

**How Diet Influences Breast Cancer Risk: Analysis of Tissue Fat, Nutrients,  
and a Dietary Pattern among High-Risk Women**

BY

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of Doctor of Philosophy.

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## **Abstract**

Background: An estimated one in eight women will develop breast cancer. Heredity, time, lifestyle, and chance determine whether and when someone develops the disease. Importantly, behavior explains the majority of the variation in breast cancer risk. Understanding how diet influences breast cancer risk empowers women with accurate information to make healthy decisions. Unfortunately, among all food, beverage, and supplement choices, there is only consensus that drinking more alcohol increases risk.

Methods: Seventy women (36 premenopausal and 34 postmenopausal) from the Breast Cancer Prevention Center, a research clinic for those with high-risk, had their benign breast tissue analyzed for evidence of cytologic atypia, which is a biomarker for short-term risk of breast cancer development. The fatty acid composition of several lipid compartments of their blood and breast tissue was analyzed by gas chromatography. Their nutrient and food consumption was estimated using the National Cancer Institute's food frequency questionnaire. The dietary differences between women with atypia and those without evidence of atypia were assessed by comparing (1) tissue fatty acid content by the Mann-Whitney U test, (2) nutrient and food intake by logistic regression after accounting for energy intake, and (3) dietary patterns derived from principal components analysis by logistic regression.

Results: Participants consumed ~10 times more n-6 polyunsaturated (PUFA) than n-3 PUFA. Compared to women without atypia, those with atypia had significantly lower n-3 PUFA in their red blood cells and circulating phospholipids, as well as lower total n-3:n-6 PUFA ratios in lipid compartments reflecting recent and long-term intake (all  $P < 0.05$ ). Among premenopausal women, greater consumption of niacin, pyridoxine, folate, vitamin B12, vitamin D,  $\alpha$ -tocopherol, selenium, n-3 PUFA, "other vegetables," fish, and soy predicted a lower likelihood

of atypia, while higher glycemic load and intake of added sugar, and trans fat were associated with evidence of atypia (all  $P < 0.05$ ). Higher intake of  $\delta$ -tocopherol and “other fruit” were associated with atypia among postmenopausal women ( $P < 0.05$ ). The protective associations of n-3 PUFA and soy intake were only detected for premenopausal participants (both  $P_{\text{interaction}} = 0.001$ ). A Modern-Traditional dietary pattern was identified, with positive scores indicating a more Traditional diet of vegetables, fish, and poultry, and negative scores reflecting a more Modern diet of grains, added sugar, trans fat, and dairy. A more Traditional dietary pattern was associated with (a) higher n-3 PUFA in blood, (b) lower n-6 PUFA in blood and breast tissue, and (c) lower levels of industrially-produced *trans* fatty acids in blood and adipose (all  $P < 0.05$ ). Each standard deviation increase in Modern-Traditional dietary pattern score was associated with 50% lower odds of atypia (95% CI: 0.26 to 0.88), with a stronger effect among younger participants (interaction for age:  $P = 0.05$ ).

Conclusions: Inadequate intake of n-3 PUFA relative to n-6 PUFA may increase the risk of developing breast cancer. Dietary intake of nutrients and foods were more strongly associated with atypia status among premenopausal compared to postmenopausal participants, particularly for n-3 PUFA and soy. A dietary pattern validated by tissue fat content was associated with short-term breast cancer risk among younger women. Taken together a diet with a higher density of nutrients from fish, poultry, and vegetables may protect against breast tumor formation, especially for younger women.

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## **Chapter One:**

### **Introduction**

### *Breast Cancer Prevention*

One in eight women will develop breast cancer at some point in life (1). The women seen at the University of Kansas Medical Center (KUMC) Breast Cancer Prevention Center (BCPC) have a higher risk than most for reasons outside of their control: mainly family history, known genetic mutations, high mammographic density, and/or breast biopsies (1). Some risk factors for breast cancer are modifiable, e.g., alcohol consumption, adult weight gain, physical inactivity, and smoking (1). Concerned women at an elevated risk have few options; they can a) opt for close surveillance, which increases the chance of finding a tumor with a better prognosis, b) surgically remove the tissue before a tumor can develop with a preventive double mastectomy, or c) take pills that manipulate estrogen signaling. As of now, selective estrogen receptor modulators (SERMs) are the only FDA-approved regimen for breast cancer risk reduction. The benefits of SERMs include fewer fractures among older women and a 50% lower incidence of estrogen-receptor positive breast cancer (2). Unfortunately, taking SERMs for breast cancer prevention does not help women live any longer (2), because they only prevent estrogen-receptor positive tumors, which they are used to treat, and SERMs carry a small risk of serious side effects like blood clots (3). Moreover, the vast majority of women estimated to benefit from SERMs do not elect to take them because they have other untoward effects that are more common, e.g., hot flashes, difficulty concentrating, and pain (2). Therefore, to make a significant impact on the incidence of breast cancer at the population level, we need to develop better ways to decrease breast cancer risk. An ideal prevention strategy has a high benefit-to-risk ratio: simple, safe, and effective.

### *Breast Cancer Risk and Dietary Recommendations*

Some of the first clues of environmental influences on breast cancer risk emerged as changing rates of incidence among immigrant offspring; after migrating from a low risk zone

(Japan) to a high risk zone (U.S.), the rate of breast cancer among second generation Japanese-Americans increased dramatically compared to their immigrant mothers (4). Dietary differences have long been hypothesized to be the most important reason why the risk of breast cancer varies across cultures (5, 6). Although much effort has been devoted to unraveling the relationship between diet and breast cancer risk, nobody has been able to demonstrate that changing dietary habits or the intake of a nutrient can significantly reduce risk. As of now, if a woman asks her doctor what she should eat (or avoid) to lower her risk, the clinician has to make suggestions without the highest form of medical evidence: demonstrated benefit from being randomly assigned to receive an intervention.

#### Randomized, Controlled Trials

The Women's Health Initiative Dietary Modification Trial randomly assigned nearly 50,000 postmenopausal women to receive a handout for U.S. dietary guidelines (control group) or participate in a behavior-change program designed to reduce fat intake to 20% of total energy by increasing consumption of fruit, vegetables, and grains (intervention group) (7). The ambitious study found multiple lines of evidence that the intervention significantly changed dietary behavior; the intervention group lost more weight and had higher blood levels of carotenoids. After 8 years of follow-up, the intervention group developed breast cancer at a 9% lower rate compared to controls, but the difference was not statistically significant; the 95% confidence interval (CI) of the hazard ratio was 0.83-1.01. Importantly, the effect of the intervention depended on the individual's baseline diet; women were most likely to benefit, i.e., exhibit a lower hazard ratio for breast cancer in the intervention group, if they were eating a) more fat or b) fewer fruit and vegetables (7). The intervention's effect also depended on tumor type; it only protected against ER+/PR- (estrogen receptor positive, progesterone receptor negative) tumors. In conclusion, the trial found that postmenopausal women may lower their risk

of developing certain types of breast cancer by consuming less fat and eating more fruit and vegetables.

The only other randomized trial for dietary prevention of breast cancer incidence included 4690 women aged 30 to 65, thereby being 73% premenopausal (8). High-risk women were eligible based on >50% mammographic density, a risk factor for breast cancer (9). The design of the trial was similar: to reduce fat intake (this time to 15% total energy) by increasing carbohydrate consumption. After an average of 10 years of follow-up, the intervention group developed breast cancer at a rate 19% higher than the comparison group, but, again, the difference was not statistically significant; the hazard ratio 95% CI was 0.91-1.55. In a reanalysis of their data, they also observed tumor-type dependent effects; higher carbohydrate intake was protective against ER+ tumors, but higher fat intake was protective against ER- tumors. Unfortunately, ER- tumors have a worse prognosis (10). To summarize this trial, initiating a low-fat diet did not lower the overall risk of developing breast cancer among a sample of mostly premenopausal women.

### Dietary Recommendations

The American Cancer Society (ACS) has taken these trials (and other studies) into consideration when crafting the following nutritional advice:

- a) maintaining a proper weight,
- b) eating a variety of 5 or more servings of fruits and vegetables each day,
- c) choosing whole grains over processed grains,
- d) eating less processed and red meat, and
- e) limiting alcohol intake to  $\leq 1$  drink per day (1).

The ACS's guidelines for the public are generally helpful for breast cancer risk reduction. The following critiques of the ACS guidelines provide the framework for illustrating the complexity of this field of research.



## Weight and Body Mass Index

First, a “proper weight” is crudely based on height; body mass index (BMI) is calculated as weight in kilograms divided by the square of height in meters;  $\leq 18.5$  is labeled as “underweight,” 18.6-24.9 “normal,” 25-29.9 “overweight,” and  $>30$  “obese.” The major limitation of using BMI is that it does not directly measure body fatness; it is a proxy (11). Given that more than 1 in 3 U.S. women are obese and another 29% overweight (12), breast cancer rates would decrease if women weighed less because being overweight or obese increases the risk of postmenopausal breast cancer (13) and breast cancer risk rises with age, with the majority of breast cancer diagnosed among postmenopausal women (14). But among premenopausal women, a higher BMI is actually associated with a lower breast cancer risk (15). Many still believe that eating fat makes you fat (because fat contains more calories per gram than carbohydrate or protein), but when obese adults are randomly assigned to dietary counseling that either promotes limiting fat intake or limiting carbohydrate intake (with no recommendation to reduce calories), the low-carbohydrate group lost more weight (~8 lbs) over a year (16).

Why does BMI exhibit opposite effects on breast cancer risk depending on menopause status? First, excessive body fat can inhibit ovulation (17) and women who ovulate less have a lower risk of breast cancer (18). Second, obesity at the end of childhood can be associated with favorable hormonal levels later, specifically lower levels of insulin-like growth factor-1 (IGF-1) in adulthood (19), which may be protective (20). Third, a low BMI also reflects greater height, and taller women are more likely to develop breast cancer (15): it is estimated that every 5 centimeter increase in height is associated with an 11% increase in risk (21).

Rather than recommending a proper weight for breast cancer risk reduction, it would be more accurate to recommend avoiding weight gain, which exhibits a stronger association with postmenopausal breast cancer risk than BMI *per se* (22). Also, since adult height is influenced by

a child's diet (23, 24), early-life eating patterns may influence breast cancer risk more than adult dietary behavior. I will later return to the concept that timing is a critical factor when considering how diet influences breast cancer risk.

### Fruits and Vegetables

On average, women who eat more fruits and vegetables tend to develop breast cancer at a lower rate compared to those who eat less (25). A recent analysis of data from nearly 1 million women followed for 11 to 20 years found that vegetable consumption is inversely associated with the development of ER- breast cancer (26). The modest protective effect of consuming more fruits and vegetables could be due to their high amount of fiber (27) and antioxidant vitamins (28). The story with fruits and vegetables seems relatively straightforward, but should they be lumped together? Do all fruits and vegetables equally modulate cancer risk? How does the method of measuring diet influence the conclusions we can draw?

The associations between vegetable intake and breast cancer risk may be distorted by the vegetables most commonly consumed: 83% of vegetables eaten by Americans are white potatoes, tomatoes (including pizza and ketchup), onions, and iceberg lettuce, compared to 6% for dark green vegetables. By consolidating vegetables into a single category, cooked spinach is equivalent to french fries! The recommendation to eat a *variety* of fruits and vegetables is supported by the observation that eating a greater diversity of vegetables is associated with a lower breast cancer risk, independent of the amount of vegetables eaten (29). Fruits and vegetables are highly diverse food groups. For example, cruciferous vegetables are rich in isothiocyanates, which up-regulate our detoxification pathways (30). Nutrient content not only varies among types of fruits and vegetables but also within a single type of fruit or vegetable; nutrient content is affected by processing and storage (31) as well as how the plants were grown (32). Lastly, potential health benefits of produce may be undermined by contamination from

pesticide residues (33) and packaging (34). These biologically relevant factors listed above, which are difficult to account for, impede our current understanding of how the consumption of fruits and vegetables influences breast cancer risk.

### Grains

Whole grains are preferred because they have not been stripped of their nutrients and fiber in the process of refinement (35). As long as a grain has not been separated into its constituents, it is considered “whole”; surprisingly, popcorn is categorized as a whole grain. Nevertheless, consuming more whole grains is considered healthy, i.e., they are often incorporated as a positive contributor to the calculation of a healthy (also called “Prudent”) diet (36, 37). Women adhering to a Prudent dietary pattern have been found to exhibit a lower breast cancer risk (reviewed more extensively below) (36). However, eating more whole grains has been associated with a higher risk of breast cancer in one population (38), although not in another (39). As of now, there is not strong evidence to suggest that eating more whole grains will reduce breast cancer risk.

The health impact of refined grains is not controversial. In fact, nutrient deficiencies only emerged as public health issues when grains began to be refined (40). Unfortunately, most grains consumed in the U.S. are refined; bread and sweetened pastries supply 1 in 7 calories for the average American adult (41). Grains constitute the greatest source of carbohydrates and breast cancer risk rises alongside a higher carbohydrate intake (42, 43), with sweet foods being particularly problematic (44). Dietary patterns that include a high intake of refined grains tend to be positively associated with breast cancer risk (45, 46). In conclusion, eating more refined grains probably increases the risk of developing breast cancer and whole grains are a better choice. However, there is no evidence to suggest that eating more whole grains will lower breast cancer risk.

## Meat

Different types of meat exhibit different health associations; women who eat more red meat and processed meat have a higher chance of dying from cancer, but the opposite is true for (non-deli) white meat (47). Meat is a major source of protein for American adults (41). Why would protein sources have varying effects on breast cancer risk? First, processed meat contains carcinogenic compounds, e.g., nitrosoamines and heterocyclic amines (48, 49). Second, red meat contains high amounts of a foreign molecule (technically, a non-human glycan) that can be incorporated into our tissue and elicits an immune response (50); this phenomenon can lead to an inflammatory process capable of promoting cancer (51). White meat does not have this unique non-human sialic acid (50). When sourcing protein from animals, women may enhance their protection against breast cancer by choosing more white meats and fish (52).

## Alcohol

Breast cancer risk rises linearly with alcohol consumption (53, 54). Dietary patterns that include high alcohol intake are also associated with a higher breast cancer risk (55-58). Although light-to-moderate drinking is associated with lower overall mortality via decreased risk of death by cardiovascular disease (59), drinking alcohol at any level is associated with higher breast cancer risk. One positive note is that alcohol only seems to aggrandize the risk of ER+ breast cancer (55, 58), for which survival is best (10).

## Fat (Lipids)

Recommendations for fat intake are conspicuously absent from the ACS dietary guidelines. There are three main categories of fat named after their chemical structure: saturated (no double bonds), monounsaturated (1 double bond), and polyunsaturated fatty acids (PUFA; at least 2 double bonds). PUFA are either n-6 ( $\omega$ -6 [omega-6]) or n-3 ( $\omega$ -3 [omega-3]). Importantly, PUFA are essential in our diet, because humans cannot make them. We can make saturated fat

and monounsaturated fat in our liver from consuming carbohydrates, especially sucrose (sugar) (60). Since we cannot make PUFA, nor can we convert n-6 to n-3 and *vice versa*, the ratio of intake is maintained in our tissue.

A recent meta-analysis found that total fat, saturated fat, and monounsaturated fat intake were not significantly associated with breast cancer risk (61). And as described above, randomized controlled trials have not confirmed the eating-more-fat-increases-breast-cancer-risk hypothesis (7, 8). However, this meta-analysis did find that women with the highest intake of PUFA have a higher risk of developing breast cancer (61). Different types of fat appear to have varying effects on breast cancer risk.

#### Polyunsaturated Fatty Acids (PUFA)

The positive association between PUFA intake and breast cancer risk could be due to linoleic acid (LA), an n-6 PUFA that now supplies about 6% of all U.S. dietary calories (62). Several groups of scientists recommend a balanced intake of n-3 and n-6 PUFA (63, 64). Among rodents, the more n-6 PUFA they are fed, the quicker and more frequently they develop mammary tumors (65). Human intake of linoleic acid has increased dramatically over the past century (66). The effects of this dietary change on breast cancer risk may not have appeared yet because they are multigenerational; the offspring of rodents fed high linoleic acid during pregnancy (*in utero* exposure) are more susceptible to mammary cancer (67-69).

The other class of PUFA, n-3, can inhibit mammary carcinogenesis in animal models, i.e., incidence (portion of sample affected), average tumor weight, and multiplicity (number of tumors per animal) (70, 71). Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are long-chain n-3 PUFA found most abundantly in the fat of some ocean fish (72); DHA can also be obtained from algae supplements (73). Among humans, a higher dietary intake of EPA and DHA is associated with a lower risk of developing breast cancer (52). As for supplementation,

U.S. women who reported regularly taking fish oil supplements had a 32% lower risk of developing breast cancer (74), but a randomized trial (designed to measure the effect on cardiovascular disease progression among older adults) found women who received EPA and DHA supplements were 3 times as likely to develop cancer (unfortunately, the authors did not specify which types of cancer) compared to those who got a placebo (75). It has been observed that n-3 PUFA consumption from food is associated with enhanced breast cancer survival, but n-3 PUFA obtained from supplements is not (76). In summary, different types of fat have effects on breast tissue that range from likely cancer-promoting (n-6 PUFA), to no measurable effect (saturated and monounsaturated), to likely protective (n-3 PUFA). And the source of n-3 PUFA may influence their effects on breast cancer risk.

#### *Methods for Measuring Diet*

As alluded to earlier, how we collect information about diet influences the data available for assessing associations with breast cancer risk. There are currently three main ways to gather information about someone's diet: dietary recalls/food records, food frequency questionnaires, and biomarkers. Dietary recalls/food records ask what foods and drinks have been consumed over 24 hours or longer. Food frequency questionnaires (FFQs) ask people to estimate how often they consume a set of food and drink items, as well as estimate the average portion size. The final method of measuring diet is to sample human tissue and measure the content of select nutrients, e.g., carotenoids in blood (77). The relative strengths and weaknesses of each method are listed in Table 1.

<i>Table 1</i> Comparison of Methods for Measuring Diet		
<b>Method</b>	<b>Strengths</b>	<b>Weaknesses</b>
Diet Recall or Food Record	- Accurate	- Diet varies day-to-day, so an accurate impression of diet patterns requires multiple days - Must be administered by trained staff - Time-intensive, especially for home-prepared food
Food	- Cheap	- Susceptible to fallacious memory: typically about

Frequency Questionnaire (FFQ)	- Do not take very long to complete	50% accurate compared to dietary recalls (78, 79) - Must be culturally sensitive and appropriate for population
Biomarkers	- Not dependent on human memory	- Expensive - Not measuring consumption, actually measuring digestion, absorption, distribution, storage, and processing. - Does not measure all parts of diet

Historically, most investigations into diet-disease connections focused on the constituents of the food, i.e., the nutrients or other biologically active components. It is important to note that for both dietary recalls and food frequency questionnaires, responses are entered into a food database that includes the nutrients and other components in foods so the estimated intake of vitamins, minerals, macronutrients (carbohydrate, fat, protein), and food groups can be determined. The nutrients in a hamburger from McDonald's are not identical to those in a 100% grass-fed hamburger grilled over an open fire and served on a fresh-baked pretzel bun, but they are both a "hamburger" in a nutrient database (different sizes can be accommodated). With their respective strengths and weaknesses, I demonstrate later how the measurement methods, in combination, can complement each other for a more accurate and complete depiction of diet.

### *Statistical Methods in Nutrition Research*

Two major statistical issues challenge nutrition research. First, people who eat healthfully tend to lead a more healthy life overall, i.e., exercise more, smoke less, and drink less alcohol (80, 81). The correlations among diet and other health behaviors make it difficult to tease apart their individual contribution toward disease risk; in statistical parlance, this problem of predictor variables being associated with each other is called "collinearity." Collinearity is also a problem within dietary measurement *per se*, because of the interrelatedness of food constituents. For example, consumption of magnesium, potassium, and dark green vegetables are all correlated with each other. The second major statistical challenge arises from the large number of foods and

nutrients that might influence disease risk; statistically comparing each one to the outcome of interest (breast cancer) increases the probability that a “significant” association will emerge by chance alone. As a convention, scientists have set the acceptable chance of making a false discovery at less than 5% for a study; this is calculated as a *P*-value. To overcome these statistical issues, researchers have begun to explore how *dietary patterns* relate to disease risk. Dietary pattern analysis aims to a) maintain the measured differences observed between participants (not throw out useful information), b) account for the interrelatedness of foods and their nutrients, and c) reduce the number of statistical comparisons with the outcome of interest.

The health effects of foods being greater than the sum of individual constituents is a concept termed “food synergy” (82). The best-known example is the Mediterranean diet (83). In a primary prevention trial for cardiovascular disease that enrolled high-risk adults, those randomized to receive personalized dietary counseling to increase adherence to the Mediterranean diet (and were given extra-virgin olive oil or nuts) were significantly less likely to develop a cardiovascular event compared to those recommended to follow a low-fat (control) diet (84). At the highest level of scientific evidence, this trial demonstrates that altering an adult’s dietary pattern can effectively slow the pathogenesis of a lifestyle-related disease.

A diet quality index is a constructed variable that (hopefully) describes the quality of one’s diet. The Mediterranean diet is an *a priori* diet quality index, i.e., calculated by an idea of what a healthy diet is. The Mediterranean diet ranges from 0 to 9; it is scored by the sum of assigning a “1” to a person each time their consumption is above their population’s median intake of a) vegetables, b) legumes, c) fruits and nuts, d) cereals (grains), e) fish, and f) ratio of monounsaturated-to-polyunsaturated fat, and if they are below the median for g) meat and h) dairy, and i) if they have moderate alcohol consumption (10-50g for males, 5-25g for females per day) (83). People with greater adherence to the Mediterranean diet have a lower risk of death,



including from (all types of) cancer (83). But reports of how the Mediterranean diet relates to breast cancer risk have been mixed; three studies found that greater adherence is associated with lower risk (45, 46), three studies reported null results (56, 85, 86), and one study found that greater adherence enhanced the likelihood of ER-/PR- tumors (87). Some of these reports attempted to parse these findings, by analyzing how each individual component influenced risk. Significantly protective foods included vegetables (46, 86), fish (86), olive oil (86), and legumes (46); conversely, greater consumption of meat and grains was positively associated with risk (46). To summarize, the Mediterranean diet has an inconsistent association with breast cancer risk, probably because it is calculated from foods with antagonistic effects.

One study exploring several *a priori* diet indices and breast cancer survival using data from the Nurse's Health Study produced a surprising finding: greater adherence to the Recommended Food Score was associated with a *higher* risk of dying from breast cancer (88). This illustrates that preconceived notions of a healthy diet can be inaccurate.

#### Multivariate-Derived Dietary Patterns

Principal components analysis (PCA) and factor analysis are two closely related multivariate techniques that generate dietary patterns from a dataset. PCA and factor analysis distill an original, large set of variables down to a smaller set of new variables that are a) uncorrelated with each other and b) represent the dimensions (continuums or axes) that best describe how subjects are different from each other (89). Multivariate-derived dietary patterns are sometimes called “empirically derived” or “*posteriori*,” because they are based on the data that was collected.

When measuring how *posteriori* dietary patterns predicted breast cancer survival in the Nurse's Health Study, investigators identified “Prudent” and “Western” dietary patterns (90). A Prudent dietary pattern was characterized by a higher intake of fruits, vegetables, low-fat dairy,

poultry, and fish, while the Western dietary pattern was characterized by a higher intake of refined grains, red meat, processed meat, high-fat dairy, and desserts. Women with a Prudent dietary pattern were 13% more likely to survive, while women with a Western dietary pattern were 15% more likely to die (90). When researchers in Cyprus found the *a priori* Mediterranean diet did not predict breast cancer risk, they analyzed their data using PCA (86). They isolated a dietary pattern indicating high consumption of fruit, vegetables, legumes, and fish (notably similar to the Mediterranean diet but not including grains, meat, alcohol, and dairy). This PCA-derived dietary pattern was strongly associated with a lower risk of breast cancer ( $p_{\text{trend}} < 0.0001$ ) with a 33% lower odds of breast cancer for women in the top quartile of this dietary pattern compared to women in the bottom quartile (86). This comparative analysis found that multivariate-derived dietary patterns could explain breast cancer risk more accurately compared to an *a priori* dietary index.

Many epidemiologists have begun to approach dietary contribution to breast cancer risk with multivariate methods. There are now 29 published studies (36, 45, 46, 55-58, 85-87, 91-109), plus 3 reviews (110-112) on the topic. The results are summarized in Figure 1. The methods and more detailed reporting of the results are available in Supplemental Tables 1 and 2.

### Statistically significant associations between dietary patterns and breast cancer risk

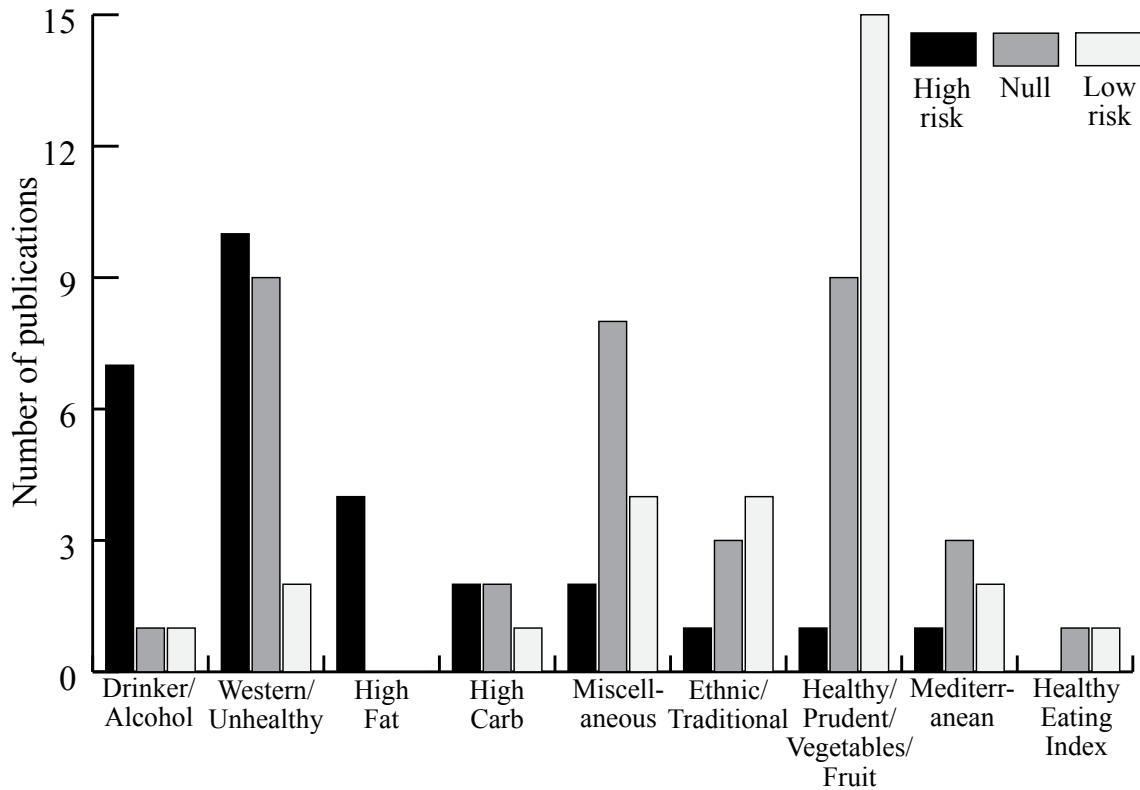


Figure 1: **Summary of Publications Relating Dietary Patterns to Breast Cancer Risk.**

Several trends emerge from this set of studies. First, Drinker/Alcohol dietary patterns are consistently associated with a higher risk of breast cancer, especially ER+/PR+ tumors. Western/Unhealthy dietary patterns are characterized by eating more high-fat dairy foods, refined grains, gravy and sauces, fast foods, red meat, processed meat, potatoes, oils, margarine, sweets and desserts, salty snacks, sodas, and added fats (112); these dietary patterns are frequently associated with a higher risk, but not consistently. The High Fat dietary patterns were consistently associated with higher breast cancer risk; importantly, all were positively loaded with meat. High Carbohydrate dietary patterns do not exhibit a discernible pattern with breast cancer risk. Ethnic/Traditional dietary patterns were often associated with reduced risk, but not consistently; the only Ethnic/Traditional dietary pattern that was positively associated with risk was notably high in meat and fried foods. Healthy/Prudent/Vegetables/Fruit dietary patterns were

defined by a higher intake of vegetables, fruits, legumes, whole grains, fish, poultry, and low-fat dairy; these dietary patterns were often associated with a lower risk of breast cancer, but, again, not consistently. The one study that found a Prudent diet associated with a higher risk of breast cancer was defined by a high intake low-fat dairy, whole grains, fruits (and fruit juice), legumes, vegetables, and soups (101). The *a priori* dietary patterns, Mediterranean and Healthy Eating Index, tended to be associated with lower breast cancer risk, but not always. One study observed a positive association between the Mediterranean diet among premenopausal women, as well as for ER-/PR- tumors (87). Finally, there were several “Miscellaneous” dietary patterns that did not fit well into the prior categories and/or were unique to the study population. Among this medley of dietary patterns, those that loaded high with meat, fat, and cheese were associated with higher risk.

Reviews of this literature have stated similar summaries. One review concluded that a diet higher in fat and sugar is associated with increased risk, while a diet high in vegetables, fruit, and white meat is associated with reduced risk (112). Another review found a) a prudent/healthy dietary pattern was associated with lower breast cancer risk, b) a drinker dietary pattern was associated with a higher risk, and c) the risk association of a Western dietary pattern was statistically non-significant (111).

A pattern of patterns is emerging. Diets dominated by high-energy, low-nutrient foods tend to positively associate with breast cancer risk, while a greater intake of low-energy, high-nutrient foods (vegetables and fruits) is negatively associated with risk of breast cancer. My work seeks to build on this research by applying a complimentary set of methods to understand how diet correlates with breast cancer risk among women seen at the BCPC.

### *Random Periareolar Fine Needle Aspiration (RPFNA)*

Risk biomarkers are valuable for studying the prevention of chronic diseases (113). A risk biomarker should be biologically relevant (mechanistically related to how the disease develops), statistically associated (predictive of disease onset or clinical progression), obtained easily, and modifiable (reversible) (113). Reversible biomarkers can be used as outcomes (surrogate endpoints) for prevention trials before embarking on trials that measure effects on incidence (113). Controlled prevention trials for chronic diseases are expensive, because they require large numbers of participants to be followed for several years. Risk biomarkers can also make intervention trials more efficient, i.e., require fewer participants, by including individuals at higher risk. Breast cancer risk biomarkers are important, because the disease develops over a long period time; for example, menarche and child birth influence the risk of developing breast cancer decades after they occur (114).

Cancer is still diagnosed with a microscope; cells within a tissue are supposed to be well organized, homogenous, and well differentiated. Abnormal cells are described as atypical; “atypia” is the presence of atypical cells. Histology is the grading of tissue normality, e.g., from excisional biopsy. Cancer risk increases in parallel with tissue abnormality in breast biopsies (115, 116). Cytology is the grading of cell normality, but without intact tissue architecture, e.g., cells collected by cervical smear (Pap test) or needle aspiration. Like histology, cytologic abnormality also correlates with risk of developing breast cancer (117). The BCPC has shown that evidence of premalignant cytology collected by random periareolar fine needle aspiration (RPFNA) is associated with the short-term risk of breast cancer (118); women with evidence of cytologic atypia are five times more likely to develop breast cancer over the next 4 years compared to women without RPFNA atypia. The prospective association between breast cancer

and atypia makes it a validated risk biomarker. Lastly, atypia can be used as a surrogate endpoint for preventive interventions, because the BCPC has demonstrated its reversibility (119).

Much of my research focuses on understanding what makes women with and without atypia different. I am specifically interested in whether dietary habits can improve our ability to predict who is likely to exhibit atypia. As a validated risk biomarker, identifying differences by atypia status sheds some light on how diet might influence breast cancer occurrence.

### *Research Questions and Gaps in the Literature*

1. What is the relationship between fat consumption and RPFNA atypia?
  - a. How is atypia associated with fat intake?
  - b. How is atypia associated with fat composition of blood and breast tissue?

There is not yet consensus on how fat consumption influences breast cancer risk. I hypothesize that the quality of fat matters more than the combined total. If the type of fat consumed differs between women with and without cytologic atypia, then the observed difference(s) may be a modifiable risk factor for development of breast cancer. Not only would the observed difference(s) be a valuable target for dietary intervention, but atypia would be a logical surrogate endpoint in a clinical trial.

2. How does nutrient intake differ between women with and without atypia?
  - a. Do the associations between nutrients and atypia depend on menopause status?

Many nutrients are thought to influence the likelihood of developing a breast tumor, but randomized controlled trials that compare supplements to placebo have not demonstrated a reduction of risk. If dietary differences can only distinguish women with and without atypia among younger, premenopausal women, then the lack of efficacy of nutrient interventions for breast cancer risk reduction may be due to timing, because all previous studies have only enrolled adult women.

3. How does the pattern of food intake differ between women with and without atypia?
  - a. What are the main ways in which women differ in their dietary habits?
  - b. Are these dietary patterns reflected in tissue fat content?
  - c. How are these dietary patterns associated with atypia status?
  - d. Do these associations depend on age or BMI?

The vast majority of women cared for at the BCPC have at least one relative that has been diagnosed with breast cancer. Dietary behavior tends to be shared among a family and may be established early in life. Given that dietary behavior may have contributed to a relative's development of breast cancer, it would be valuable to define the major dietary patterns of these U.S. Midwestern women with an elevated risk of breast cancer.

Tissue fatty acids are biomarkers of dietary behavior, i.e., especially PUFA since they must be consumed. If tissue fatty acid levels are correlated with a dietary pattern(s), then the dietary pattern's legitimacy as a measure of actual behavior is strengthened. And if the dietary pattern can distinguish women with and without atypia, then it may influence the risk of developing breast cancer risk and could be targeted in a clinical trial using atypia as a surrogate endpoint. And if the associations between the dietary pattern and atypia differ for older versus younger women, or skinnier versus heavier, then such differences should be taken into account when designing the clinical trial.

## **Chapter Two:**

### **Subjects and Methods**



### *Eligibility*

Between June 2009 and February 2010, all women undergoing RPFNA at the BCPC were invited to provide a blood sample and information about dietary intake. All potential recruits had already agreed to participate in a prospective study evaluating the prospective value of biomarkers among women at higher than normal risk for developing breast cancer. Women were eligible for RPFNA on the basis of any of the following: (a) an affected close relative under the age of 60, (b) a prior breast biopsy revealing atypical hyperplasia, lobular carcinoma in situ, ductal carcinoma in situ (DCIS), or prior invasive breast cancer (if there is a history of DCIS or invasive cancer, only the contralateral breast is sampled), (c) multiple breast biopsies, (d) atypia found on a previous RPFNA, or (e) >50% radiographic breast density. Participants were excluded if they had breast implants, were taking potent anticoagulants, had taken chemotherapy or endocrine therapy within 12 months, or were currently enrolled in an interventional clinical trial. Participants read and signed an informed consent document approved by KUMC's institutional review board, the Human Subjects Committee.

### *Breast Cancer Risk and Anthropometrics*

Prior to visiting our clinic, information was collected from participants by phone to calculate breast cancer risk using the Gail risk model (120). The Gail risk model is calculated from current age, age of menarche, age at birth of the first child (or nulliparous), family history of breast cancer, number of breast biopsies, finding atypical hyperplasia in a breast biopsy, race, and ethnicity. In the clinic, height and weight were measured.

### *Specimen Acquisition*

Blood was drawn after a 12-hr fast and separated into plasma, buffy coat, and RBC. Samples were placed on ice until they were stored at -80°C. Blood samples were not necessarily obtained the same day as the RPFNA, because RPFNA is not performed fasting.

In order to control for how breast tissue varies with the menstrual cycle, RPFNA was performed during the follicular phase (days 1-10) for premenopausal women. Women were asked not to take any n-3 PUFA supplements or non-steroidal anti-inflammatory drugs for three weeks prior to the procedure to reduce the risk of bleeding complications. In RPFNA, each breast is sampled at two sites under local anesthesia. Samples from both breasts are pooled together in an isotonic solution, immediately frozen in liquid nitrogen, and transferred to a -80°C freezer within 12 hours. The frozen tissue was later thawed, mixed in an ice bath and realiquoted into four cryovials, with one designated for fatty acid analysis.

### *Tissue Processing*

#### Cytology, Cytomorphology, and Proliferation Rate

The remaining RPFNA material (after aliquoting for cryovial storage) was prepared to assess cytology assessment and cell proliferation rate by immunocytochemistry (119). A single cytopathologist, who did not have access to results from diet and tissue fatty acid measurements, scored specimens using categorical cytology descriptions of (a) normal non-proliferative, (b) hyperplasia, and (c) hyperplasia with atypia. Specimens were also given a cytomorphology score, referred to as a Masood score (121); scores of 11-14 correspond to hyperplasia, scores of 15-18 hyperplasia with atypia, and 19-24 as suspicious for malignancy (121, 122). The number of epithelial cells per slide were categorized into the following ranges: <10, 10-99, 100-499, 500-999, 1000-5000, or >5000.

The immunocytochemistry process involves staining for the presence of Ki-67 protein, which identifies the cells that are dividing (123). Cell clusters containing the highest proportion of cells staining positive for Ki-67 were preferentially counted. Two independent readers recorded the number of positive-staining nuclei out of 500. In case of a difference between the

two readers, the scores were averaged. Ki-67 was not performed on specimens with <500 cells per slide; instead, Ki-67 was imputed as zero.

### Tissue Fatty Acids

We measured the fatty acid composition of red blood cell (RBC) phospholipids (PLs), plasma PLs, plasma TAGs, breast PLs, and breast TAGs using a modified Folch method (124). Different lipid compartments indicate fat intake over different lengths of time; plasma triacylglycerides reflect fat intake over the previous hours to days, plasma phospholipids days to weeks, erythrocyte phospholipids weeks to months, and breast triacylglycerides months to years (125). Briefly, hydrophobic extracts of plasma and breast tissue were separated into PLs and TAGs by solid-phase chromatography (126). After transmethylation with boron trifluoride-methanol, fatty acid methyl esters were isolated and analyzed by gas chromatography using a Varian 3900 (Agilent Technologies, Santa Clara, CA, USA) with helium as the carrier gas and reported as weight percent of total fatty acids (127).

### *Food Frequency Questionnaire*

Participants were asked to complete a paper copy of the original DHQ-I (Appendix 1) and return it by mail. The DHQ-I is a food frequency questionnaire developed by the National Cancer Institute (NCI). The survey asks about average consumption of >200 foods, beverages, and nutritional supplements with >400 questions (128). Responses to the multiple-choice questions were entered into Diet\*Calc version 1.4, an online software program developed by the NCI to analyze the DHQ-I. Input was computed into average daily nutrient intake using calculations from the Nutritional Data System for Research (NDS-R) and United States Department of Agriculture (USDA) National Nutrient Database for Standard Reference, release 22. The output of most dietary parameters (123 of 131) was as weight or servings per day. Other

output variables included daily glycemic load, daily energy intake, and the percent energy contribution of macronutrients. All output variables are listed in Supplemental Table 3.

### *Statistical Analyses*

Analyses were performed using JMP version 11.0.0 (SAS Institute). All tests were set at a two-sided false discovery rate of less than 5% without correction for multiple comparisons.

#### Fat Intake and Atypia

Except for a few exceptions, fatty acid intakes and tissue content of fatty acids did not exhibit normal distributions; therefore, the differences between women with and without atypia (independent variable) were assessed by the Mann-Whitney U test, a non-parametric comparison of continuous variables (dependent variables) between two groups. The results of these analyses are presented as medians, inter-quartile ranges (IQR), and *P*-values.

#### Individual Dietary Parameters and Atypia

The distribution of all raw output was assessed for normality using the Shapiro-Wilk test and log-transformed as necessary. Nutrients, food and food groups were adjusted for energy intake using the residual method developed by Willett and Stampfer (129). The method is illustrated and explained in Figure 2. Since the energy-adjusted variables represent relative intake, they were standardized, i.e., converted into Z-scores, to make them comparable with each other.

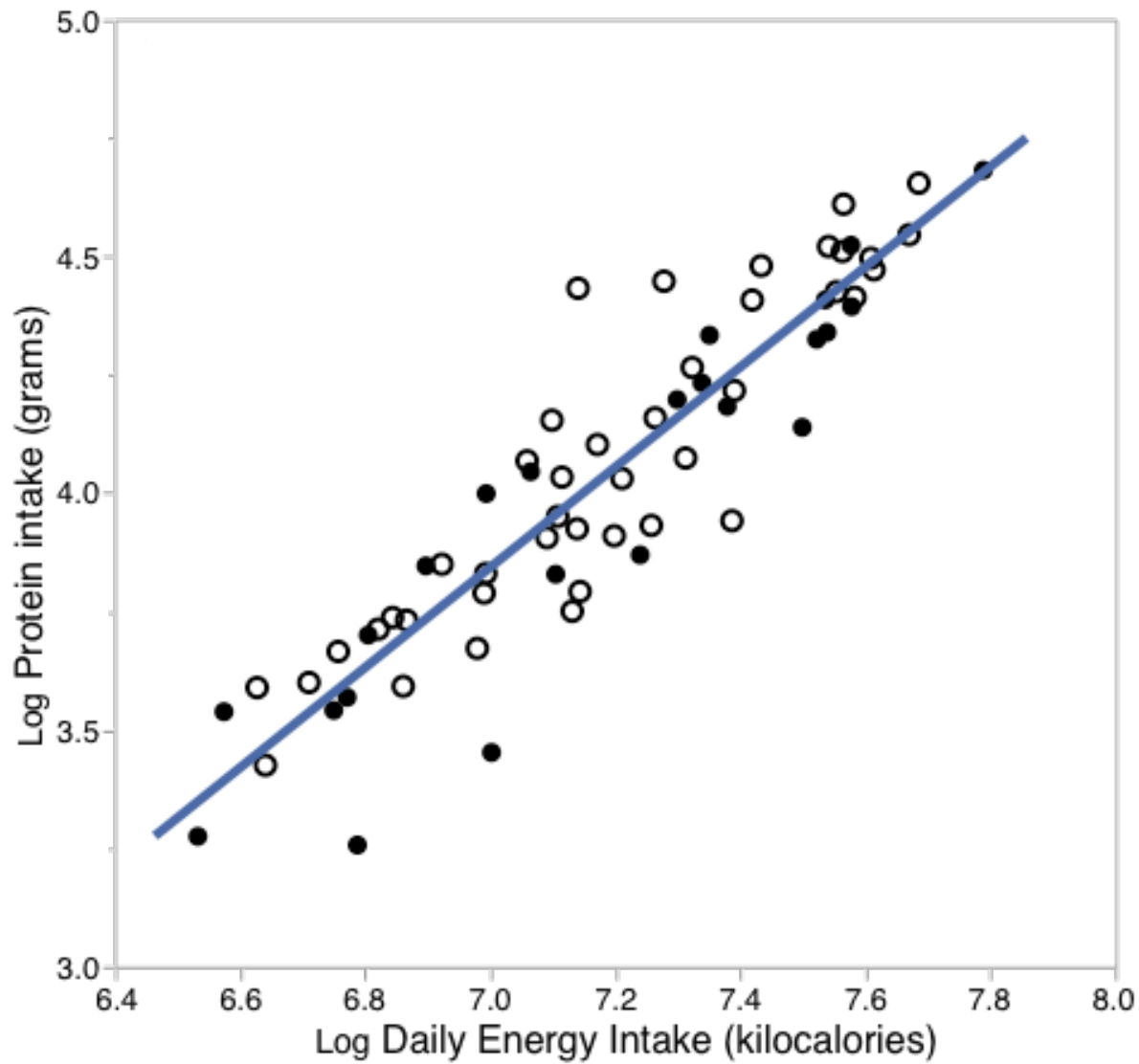


Figure 2: **Energy Adjustment Using the Residual Method.** The blue line indicates the line of best fit for a nutrient (dependent variable on the Y-axis) by energy (independent variable on the X-axis). A residual is the vertical distance between a point and the blue line; therefore, a positive residual indicates the individual consumed more of the nutrient than average for her energy intake. Residuals convey relative intake or nutrient density. The white circles represent women without RPFNA atypia, the filled circles women with atypia.

The association between nutrients and breast cancer risk status (cytology) was measured by logistic regression. Nutrient intake was used as the independent variable with cytology (non-proliferative or hyperplasia without atypia *versus* hyperplasia with atypia) as the dependent variable. Associations between nutrients and atypia were measured separately for premenopausal and postmenopausal participants. An interaction term formally tested whether the association

between a nutrient and cytology differed by menopause status. Results are presented as odds ratios of atypia (with 95% confidence interval [CI]) per Z-score increase of nutrient intake. An odds ratio is the probability of something being true divided by the probability of something not being true. A final model was selected by forward stepwise regression separately for premenopausal and postmenopausal women.

### Dietary Patterns and Atypia

Principal components analysis (PCA) was performed on the correlation matrix of dietary parameters, e.g., kilocalories, macronutrients, micronutrients, food groups, glycemic load, alcohol, and proportion of energy from macronutrients. To reiterate, PCA is a multivariate technique that consolidates correlated continuous variables into fewer, uncorrelated factors that reveal the internal structure of the data. The number of factors to retain for analysis was decided by the Scree test, which uses visual inspection to select the cut-point whereat small differences in eigenvalues begin. A recent methods report found a 3-component solution for PCA of diet identified by the Scree test to be most reproducible (130).

Biological evidence of fat consumption within dietary patterns was measured by correlating the dietary patterns with fatty acids in tissue samples. The associations were measured using Spearman's rank correlation coefficient to account for non-normal distributions.

The association between PCA-derived dietary patterns and RPFNA atypia was assessed by simple logistic regression. Dietary patterns were tested for an interaction with menopause status, age, and body mass index ( $\text{kg}/\text{m}^2$  [BMI]). *P*-values for interactions are presented along with results from stratified analyses by menopause status, above/below median age, and above/below median BMI.

## **Chapter Three:**

### **Low Levels of n-3 PUFA and Low n-3:n-6 PUFA Ratios in Blood and Breast Tissue are Associated with Cytologic Atypia**

Adapted from “Omega-3 and Omega-6 Fatty Acids in Blood and Breast Tissue of High-Risk Women and Association with Atypical Cyтомorphology” *Cancer Prevention Research*, 2015.

### *Abstract*

Background: The ratio of n-3 to n-6 PUFA is inversely associated with breast cancer risk. We measured the association between cytologic atypia, a biomarker for short-term risk of breast cancer development, and n-3 and n-6 PUFA intake and levels in blood and breast tissue.

Methods: Blood and benign breast tissue, sampled by RPFNA, was obtained from 70 women at elevated risk for breast cancer. Participants completed the National Cancer Institute's FFQ in order to assess dietary fat intake. The fatty acid composition of five lipid compartments, red blood cell, plasma and breast phospholipids (PLs) and plasma and breast triacylglycerides (TAGs), were analyzed by gas chromatography. Differences between groups were assessed by the Mann-Whitney U test.

Results: The median total n-3:n-6 intake ratio was 1:10. Compared to women without atypia, those with cytologic atypia had significantly lower total n-3 PUFA in red blood cell and plasma PLs and lower total n-3:n-6 ratios in plasma TAGs and breast TAGs ( $p < 0.05$ ).

Conclusion: This is the first report of associations between tissue levels of n-3 and n-6 PUFA and a reversible tissue biomarker of breast cancer risk. Therefore, RPFNA cytology could serve as a surrogate endpoint for breast cancer prevention trials of long-chain n-3 PUFA supplementation.



### *Introduction*

The ratio of n-3:n-6 PUFA intake translates into differences in blood and breast tissue, because are entirely derived from diet (125). The majority of n-3 and n-6 PUFA consumed are the 18-carbon essential fatty acids, alpha-linolenic acid (ALA) and linoleic acid (LA). ALA and LA share enzymes that convert them into long-chain (20- and 22-carbon) fatty acids (Figure 3).

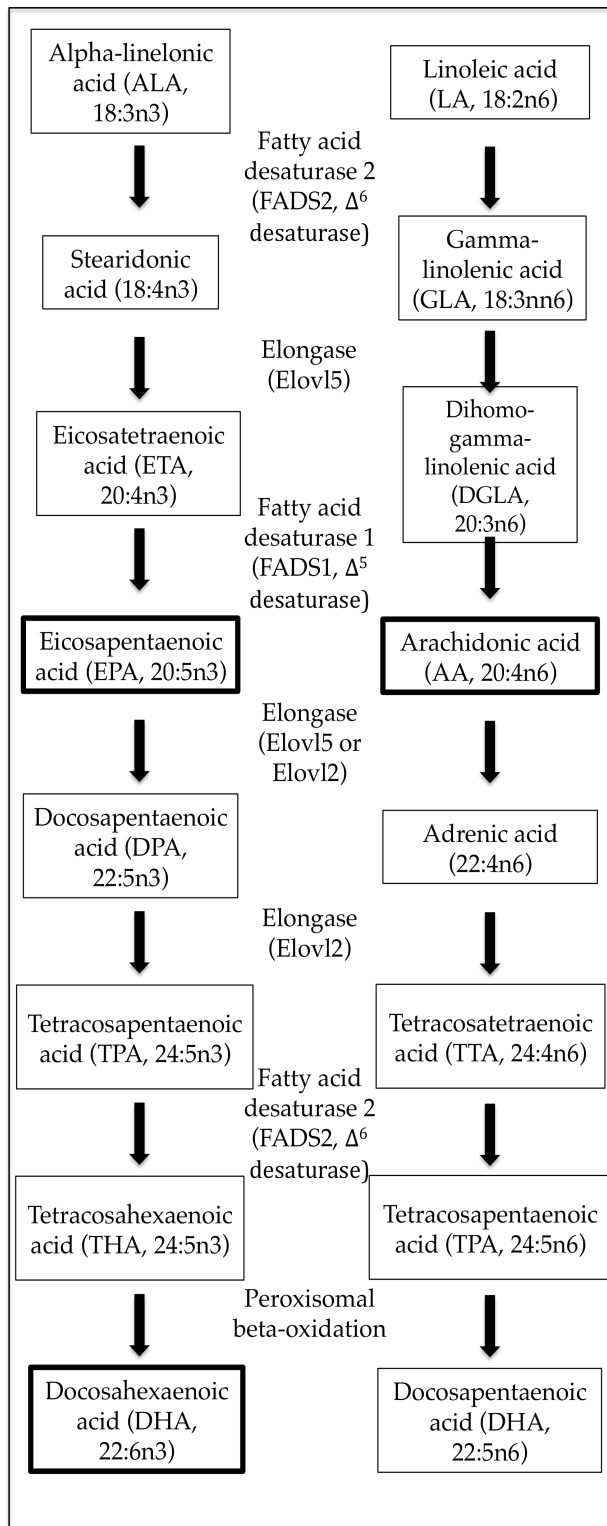


Figure 3: **Polyunsaturated Fatty Acid Elongation and Desaturation.** Fatty acids are in boxes. Enzymes are in the center. Arachidonic acid, EPA, and DHA are thickly bolded, because they are the most physiologically potent PUFA. The first elongation and desaturation steps likely occur in reverse order as well.

Arachidonic acid (AA), the predominant long-chain n-6 PUFA, is a key component of plasma membrane phospholipids (PLs), from where it can be released and converted into potent pro-inflammatory eicosanoids by cyclooxygenase (COX) and lipoxygenase (LOX) enzymes (64, 131). EPA and DHA, the primary long-chain n-3 PUFA, decrease inflammation by (a) competing with AA as enzymatic substrates and (b) serving as precursors of resolvins and protectins, which terminate inflammatory processes (132, 133).

A low n-3 PUFA intake relative to n-6 PUFA may contribute to breast cancer risk, because a low n-3:6 PUFA ratio in tissue can create a pro-inflammatory milieu (64, 131), which promotes tumor formation and progression (134). The effect of n-3 and n-6 PUFA intake on breast cancer risk in humans has been extensively studied, but not yet determined (52, 135). This research is complicated by the accuracy of assessing intake with FFQs (136) and inconsistent results among different populations (52, 137).

Compared to controls, women with breast cancer tend to have lower EPA and DHA in their red blood cells (RBC) (138, 139). Prospective studies observe an inverse association between consumption of EPA and DHA and breast cancer incidence (52). However, the fatty acid content of blood taken from women *before* they develop breast cancer does not differ (in EPA, DHA, or total n-3 PUFA levels) from women that do not go on to develop breast cancer (140-146).

In this cross-sectional study, we measured the association between fatty acid content in blood and benign breast tissue samples and cytologic atypia (118). We hypothesized that women with (a) lower intakes and (b) levels of n-3 PUFA relative to n-6 PUFA in their tissue would be more likely to exhibit RPFNA atypia.

## *Materials and Methods*

### Eligibility

Between June 2009 and February 2010, all women undergoing RPFNA at the BCPC were invited to provide a blood sample and information about dietary intake. All potential recruits were already participants in an ongoing study evaluating the prospective value of biomarkers among women at higher than normal risk for developing breast cancer. Women were eligible for RPFNA on the basis of any of the following: (a) an affected close relative under the age of 60, (b) a prior breast biopsy revealing atypical hyperplasia, lobular carcinoma in situ, ductal carcinoma in situ (DCIS), or prior invasive breast cancer (if there is a history of DCIS or invasive cancer, only the contralateral breast is sampled), (c) multiple breast biopsies, (d) atypia found on a previous RPFNA, or (e) >50% radiographic breast density. Participants were excluded if they had breast implants, were taking potent anticoagulants, had taken chemotherapy or endocrine therapy within 12 months, or were currently enrolled in an interventional clinical trial. Participants read and signed an informed consent document approved by KUMC's institutional review board, the Human Subjects Committee.

### Food Frequency Questionnaire

Dietary fat intake was assessed by the diet history questionnaire (DHQ-I), a FFQ developed by the National Cancer Institute (128). The DHQ-I asks women to reflect on their normal diet, querying how much they consume various foods, drinks, and dietary supplements.

### Specimen Acquisition and Processing

Blood was drawn after a 12-hr fast and separated into plasma, buffy coat, and RBC. Samples were placed on ice until they were stored at -80°C. Blood samples were not necessarily obtained the same day as the RPFNA, because RPFNA is not performed fasting.

In order to control for how breast tissue varies with the menstrual cycle, RPFNA was performed during the follicular phase (days 1-10) for premenopausal women. Women were asked not to take any n-3 PUFA supplements or non-steroidal anti-inflammatory drugs for three weeks prior to the procedure to reduce the risk of bleeding complications. In RPFNA, each breast is sampled at two sites under local anesthesia. Samples from both breasts are pooled together in an isotonic solution, immediately frozen in liquid nitrogen, and transferred to a -80°C freezer within 12 hours. The frozen tissue was later thawed, mixed in an ice bath and realiquoted into four cryovials, with one designated for fatty acid analysis.

The remaining RPFNA material (after cryovial storage) was prepared to assess cytology assessment and cell proliferation (119). A single cytopathologist, who did not have access to results from diet and tissue fatty acid measurements, scored specimens using categorical cytology descriptions of (a) normal non-proliferative, (b) hyperplasia, and (c) hyperplasia with atypa. Specimens were also given a cytomorphology score, referred to as a Masood score (121); scores of 11-14 correspond to hyperplasia, scores of 15-18 hyperplasia with atypia, and 19-24 as suspicious for malignancy (121, 122).

The immunocytochemistry process involves staining for the presence of Ki-67 protein, which identifies the cells that are dividing (123). Proliferation measurement involves categorizing the number of epithelial cells per slide into the following ranges: <10, 10-99, 100-499, 500-999, 1000-5000, or >5000. Cell clusters containing the highest proportion of cells staining positive for Ki-67 were preferentially counted. Two independent readers recorded the number of positive-staining nuclei out of 500. In case of a difference between the two readers, the scores were averaged. Ki-67 was not performed on specimens with <500 cells per slide; instead, Ki-67 was imputed as zero.

### Tissue Fatty Acid Measurement

We measured the fatty acid composition of RBC PLs, plasma PLs, plasma TAGs, breast PLs, and breast TAGs using a modified Folch method (124). Briefly, hydrophobic extracts of plasma and breast tissue were separated into PLs and TAGs by solid-phase chromatography (126). After transmethylation with boron trifluoride-methanol, fatty acid methyl esters were isolated and analyzed by gas chromatography using a Varian 3900 (Agilent Technologies, Santa Clara, CA, USA) with helium as the carrier gas and reported as weight percent of total fatty acids as previously described (127).

### Statistical Analysis

Analyses were performed using JMP version 11.0.0 (SAS Institute). The medians, inter-quartile ranges (IQR), and *P*-values are presented. Non-parametric analyses were chosen to account for the non-normal distributions of variables. All tests were set at a two-sided false discovery rate of less than 5%. No corrections for multiple comparisons were made.

## *Results*

### Study Participation

Between June 2009 and February 2010, 142 women underwent RPFNA at the BCPC, of which 110 met the criteria for eligibility. Seventy (N=70) agreed to complete the DHQ-I and to have additional fasting blood obtained for fatty acid analysis. Sixty-two of 70 women (89%) completed and returned the DHQ-I. About half of the RPFNA samples contained adequate breast tissue for fatty acid analysis: breast PLs (N=43); breast TAGs (N=40); breast PLs or breast TAGs (N=49); both breast PLs and breast TAGs (N=34) (Figure 4).

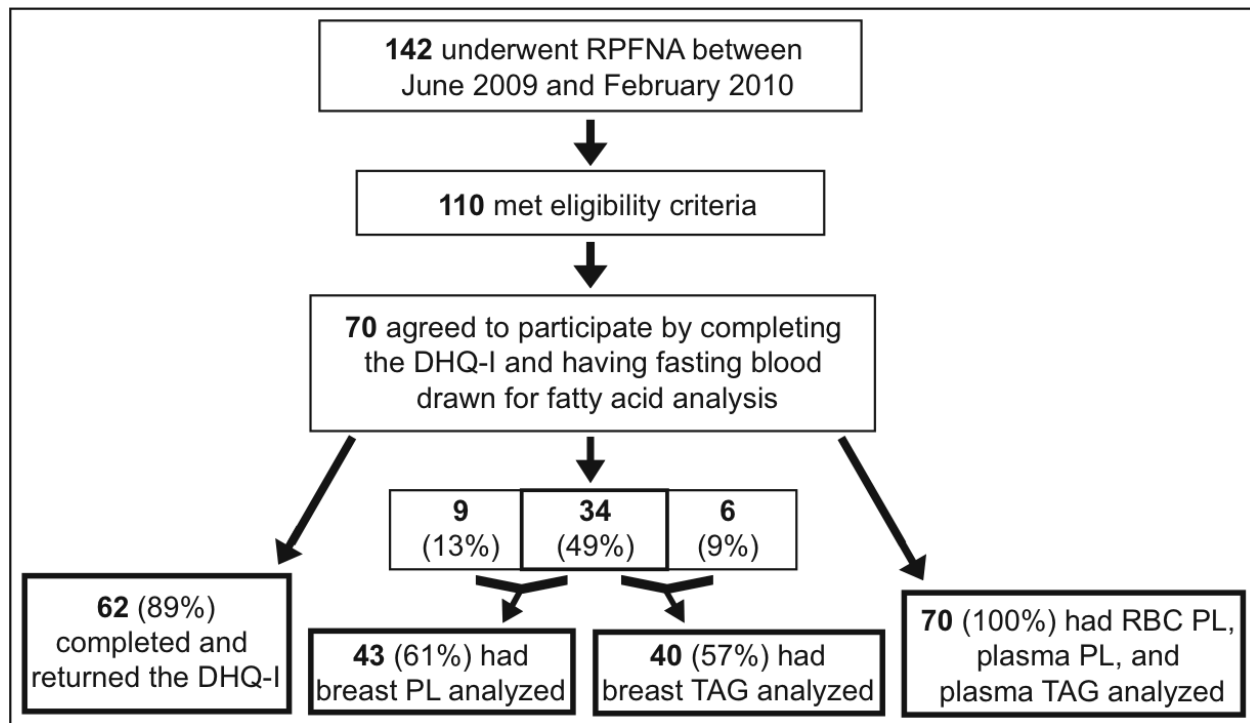


Figure 4: **Consort Diagram of Participation and Data Availability.** The boxes with bolded borders represent the data that was included in the final analysis.

Nearly all of the participants were Caucasian (96%), 50% had a college degree, and 70% reported an income of >\$60,000 per year. In 2010, the median household income in the U.S. was \$49,445. Fifty-one percent were premenopausal and 83% of those took oral contraceptives. Almost all postmenopausal women used some type of hormonal supplementation (91%). Twenty-three percent took fish oil supplements until discontinuing use at least 3 weeks prior to their RPFNA. The median (IQR) risk of developing breast cancer over the next 5 years, according to the Gail model (120), was 2.3% (1.2 to 3.5%). Nine in 10 participants had a family history of breast cancer. Median BMI was 24.5 (22.2 to 27.6) kg/m<sup>2</sup>. Twenty-six participants (37%) exhibited hyperplasia with atypia and the overall median Ki-67 was 0.9% (0.0 to 3.3%).

#### Characteristics of Women with and without Cytologic Atypia

Table 2 compares demographic and risk characteristics between women with and without atypia. As expected, women with cytologic atypia had higher Masood scores ( $p < 0.0001$ ) and

higher rates of proliferation ( $p=0.0004$ ). Women with cytologic atypia were taller ( $p=0.01$ ) than those without atypia, but both groups had similar BMI.

<i>Table 2 Participant Characteristics by Evidence of Atypia in RPFNA</i>				
	Overall (n=70)	No atypia (n=44)	Atypia (n=26)	<i>P</i> -value
Median (Interquartile Range) or Number (Percent)				
Age (yrs)	48 (43-56)	48 (43-56)	45 (42-55)	0.48
Height (cm)	164 (161-169)	164 (160-167)	166 (163-173)	0.01
Weight (kg)	67 (62-77)	66 (62-77)	67 (61-78)	0.60
BMI (kg/m <sup>2</sup> )	25 (22-28)	25 (22-29)	24 (22-27)	0.57
<sup>a</sup> 5yr Gail risk (%)	2.3 (1.2-3.5)	2.4 (1.3-3.3)	1.8 (1.1-3.7)	0.96
Masood score	14 (13-15)	13 (12-14)	16 (15-16)	<0.0001
<sup>b</sup> Ki-67 (%)	0.9 (0.0-3.3)	0.4 (0.0-2.4)	2.7 (0.9-5.6)	0.0004
Premenopausal	36 (51%)	21 (48%)	15 (58%)	0.47
OC use	30 (83%)	18 (86%)	12 (52%)	0.68
Postmenopausal	34 (49%)	23 (52%)	11 (42%)	0.47
HRT use	31 (91%)	20 (87%)	11 (48%)	0.54
Family History (+)	63 (90%)	38 (86%)	25 (96%)	0.25
<sup>c</sup> Fish oil	14 (23%)	11 (28%)	3 (14%)	0.21

Abbreviations: Body mass index (BMI), oral contraceptive (OC), hormone replacement therapy (HRT). *P*-values were calculated by Pearson's Chi-Squared and the Mann-Whitney U tests. <sup>a</sup>The 5yr Gail risk estimates an individual's risk of developing breast cancer over the next five years based on family history, known genetic mutations, reproductive history, and breast biopsies (120). <sup>b</sup>For the 12 women whose RPFNA contained <500 cells on the slide, Ki-67 was not performed and a value of 0% was imputed. <sup>c</sup>Fish oil use was measured by the DHQ, thus n=62.

### Atypia and Fatty Acid Dietary Intake

The median total intake of long-chain n-3 PUFA (EPA+DHA) was 55mg (30 to 123mg) per day (Table 3). There was no statistically significant difference between women with and



without atypia for dietary intake of the individual fatty acids EPA, DHA, and AA. The median total n-3:n-6 intake ratio of women without atypia was not greater than that of women with atypia (0.11 vs. 0.10,  $P=0.30$ ). However, when including fish oil supplements, the intake ratio of EPA+DHA:AA was lower among women with atypia ( $P=0.03$ ).

<i>Table 3</i> Estimated Fat Intake (grams/day) by Evidence of Atypia in RPFNA			
	No atypia (n=40)	Atypia (n=22)	P-value
	Median (Interquartile Range)		
<u>Total fat</u>	50 (34-62)	51 (35-60)	0.90
Saturated	15 (11-19)	15 (12-20)	0.73
Monounsaturated	20 (13-25)	19 (14-23)	0.98
Trans	2.0 (1.4-2.7)	2.4 (2.0-3.3)	0.08
n-3 and n-6 PUFA	12 (7.6-15)	9.9 (7.2-13)	0.27
<u>Dietary n-6 PUFA</u>	11 (6.7-14)	8.9 (6.5-12)	0.25
LA (18:2n6)	10 (6.6-14)	8.8 (6.5-12)	0.25
AA (20:4n6)	0.08 (0.05-0.10)	0.08 (0.06-0.13)	0.79
<u>Dietary n-3 PUFA</u>	1.06 (0.80-1.3)	0.84 (0.62-1.2)	0.13
ALA (18:3n3)	0.98 (0.72-1.2)	0.76 (0.61-1.0)	0.14
EPA (20:5n3)	0.02 (0.01-0.04)	0.01 (0.00-0.03)	0.24
DHA (22:6n3)	0.04 (0.02-0.09)	0.03 (0.02-0.08)	0.33
EPA + DHA	0.06 (0.03-0.13)	0.04 (0.02-0.10)	0.31
<sup>a</sup> <u>Total n-3 PUFA</u>	1.2 (0.94-1.5)	0.86 (0.62-1.4)	0.15
Total EPA	0.04 (0.01-0.21)	0.02 (0.00-0.07)	0.09
Total DHA	0.08 (0.03-0.15)	0.04 (0.02-0.11)	0.13
Total EPA+DHA	0.12 (0.05-0.33)	0.06 (0.02-0.19)	0.11
<u>Ratios</u>			
Dietary (EPA+DHA)/AA	0.80 (0.46-1.2)	0.57 (0.26-1.1)	0.14
Total (EPA+DHA)/AA	1.4 (0.75-3.8)	0.70 (0.33-1.9)	0.03
Dietary n-3:6 PUFA	0.10 (0.090-0.12)	0.10 (0.092-0.10)	0.52
Total n-3:6 PUFA	0.11 (0.092-0.13)	0.10 (0.092-0.12)	0.30

Abbreviations: Linoleic acid (LA), arachidonic acid (AA), alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). <sup>a</sup>Total includes fish oil supplementation in addition to dietary intake. P-values were calculated by the Mann-Whitney U test.

### Atypia and Fatty Acids in Blood and Breast Tissue

There were no significant differences between women with and without atypia for any n-6 PUFA ( $P>0.05$ ). EPA was lower in the plasma PLs and plasma TAGs of women with atypia ( $P<0.05$ ). DHA was also lower among women with atypia in RBC PLs and plasma TAGs ( $P<0.05$ ). Another long-chain n-3 PUFA, docosapentaenoic acid (DPA n-3), was lower among women with atypia in plasma TAGs and breast TAGs ( $P\leq 0.05$ ). Total n-3 PUFA was lower among women with atypia in RBC PLs and plasma PLs ( $P<0.05$ ).

The difference in n-3:n-6 ratios are presented in Figure 5. The EPA+DHA:AA ratio was lower in the plasma TAGs of women with atypia compared to those without atypia ( $P=0.05$ ). The total n-3:n-6 PUFA ratio was lower in both plasma TAGs and breast TAGs ( $P<0.05$ ) of women with atypia compared to women without atypia.

All comparisons (medians and exact  $P$ -values) of each fatty acid and PUFA ratio between women with and without RPFNA atypia are available in Supplemental Tables 4-8.

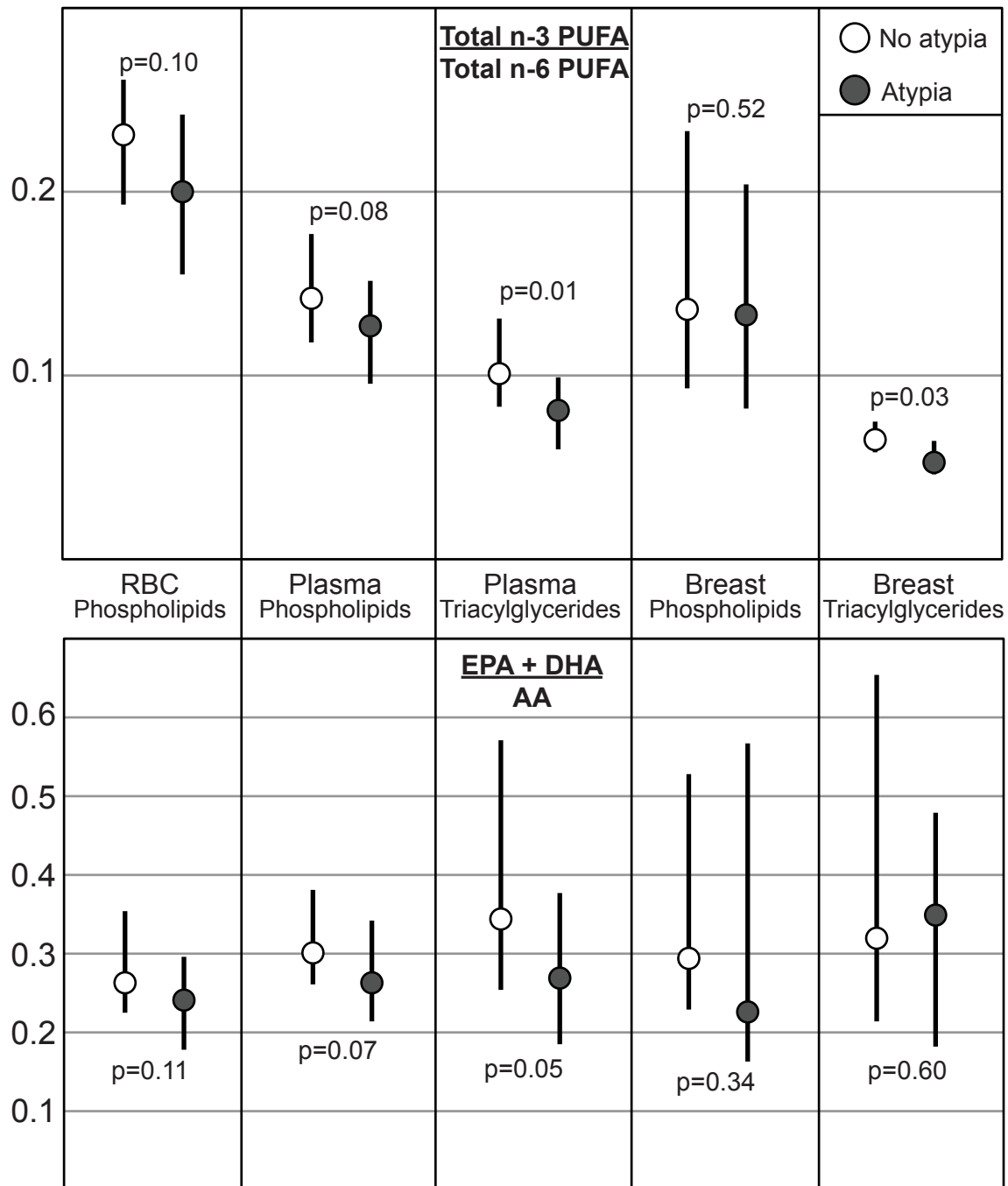


Figure 5: **N-3:N-6 PUFA Ratios in Blood and Breast Tissue of Women with and without RPFNA Atypia.** Medians and interquartile ranges are depicted as circles and error bars, respectively. P-values were calculated by the Mann-Whitney U test.

## Breast Epithelial Cell Characteristics and Fatty Acids

Table 4 lists significant correlations identified between proliferation rate or cytology index (Masood score) and several PUFA. The proliferation rate of breast epithelial cells was positively correlated with levels of LA and AA in breast PLs (n-6 PUFA) ( $P<0.05$ ). Proliferation rate was negatively correlated with EPA in RBC PLs and AA in breast TAGs ( $P<0.05$ ). The Masood score was negatively correlated with DPAn-3 in RBC PLs, plasma PLs, and breast TAGs ( $P<0.05$ ). Lastly, the total n-3:n-6 PUFA ratio in breast TAGs was negatively correlated with Masood score ( $P=0.001$ ).

<i>Table 4</i> Significant Correlations between Tissue n-3 PUFA and n-6 PUFA and Breast Epithelial Proliferation Rate and Cytomorphology			
Lipid compartment	Fatty acid or ratio	Spearman's rho	<i>P</i> -value
Correlations with proliferation rate (%Ki-67)			
RBC PL	EPA	-0.26	0.03
Breast PL	LA	0.32	0.04
	AA	0.34	0.03
Breast TAG	AA	-0.33	0.04
Correlations with cytomorphology (Masood score)			
RBC PL	20:2n6	0.27	0.02
	22:2n6	-0.28	0.02
	DPAn-3	-0.24	0.04
	AA	-0.28	0.02
Plasma PL	DPAn3	-0.25	0.03
	EPA	-0.24	0.04
Plasma TAG	EPA	-0.24	0.05
Breast TAG	LA	0.32	0.05
	22:4n6	-0.40	0.01
	DPAn3	-0.49	0.001
	n-3:n-6	-0.49	0.001

## *Discussion*

In our sample of women with an elevated risk for breast cancer development, consumption of total n-3 relative to n-6 PUFA was about 1:10, much lower than the recommendation for 1:2 (62). Although not statistically significant, women with atypia consumed half as much EPA and DHA compared to women without atypia. In blood and breast tissue, we found a pattern of lower levels of n-3 PUFA of women with atypia compared to those without.

These results are consistent with studies that find lower EPA, DHA, and n-3:n-6 ratios in RBCs (138, 139) and adipose tissue (147, 148) from women with breast cancer compared to controls. Long-chain n-3 PUFA are especially prone to oxidation (149); therefore, the non-correlations of n-3 PUFA in blood and tissue and breast cancer risk in nested, case-control studies (140-146) may be due to degradation of samples stored for 4 to 25 years (143, 145).

Tissue DPAn-3 repeatedly emerged as a significant predictor of cytology atypia, Masood index, and proliferation rate. Higher concentrations of DPAn-3 may reduce breast cancer risk, because (a) it can be converted into anti-inflammatory mediators like EPA and DHA (150), (b) higher levels in circulation is associated with lower systemic inflammation (151), and (c) DPAn-3 induces mammary gland differentiation (152). The role of DPAn-3 in breast carcinogenesis merits more investigation.

The results of this study incite two general conclusions and a hypothesis. First, women consuming their usual diet in the Midwest U.S. have a low intake of n-3 PUFA relative to n-6 PUFA, which is reflected in their blood and breast tissue. Second, we found inverse associations between tissue levels of long-chain n-3 PUFA and n-3:n-6 ratios and a reversible risk biomarker of breast cancer. Others have shown that high-dose supplementation of long-chain n-3 PUFA is a safe and effective method of increasing their tissue concentration (153); therefore, we

hypothesize that supplementation of long-chain n-3 PUFA may correct cytologic abnormalities in breast tissue by balancing the ratio n-3 PUFA relative to n-6 PUFA.

## **Chapter Four:**

### **Dietary Associations with Cytologic Atypia in Breast Tissue of Women with Elevated Risk Differ by Menopause Status**



### *Abstract*

Purpose: To better understand how diet influence risk for developing breast cancer.

Methods: Thirty-three premenopausal and 32 postmenopausal women with an elevated risk of developing breast cancer completed the National Cancer Institute's FFQ. Estimated intakes were adjusted for energy. Benign breast tissue was obtained by RPFNA for evaluation of cytologic atypia, a known breast cancer risk biomarker. The associations between nutrients and atypia were assessed using logistic regression.

Results: Among premenopausal women, greater consumption of niacin, pyridoxine, folate, vitamin B12, vitamin D,  $\alpha$ -tocopherol, selenium, n-3 PUFA, "other vegetables," fish, and soy predicted a lower likelihood of atypia, while higher glycemic load and intake of added sugar, and trans fat was associated with evidence of atypia (all  $P < 0.05$ ). Only  $\delta$ -tocopherol and "other fruit" were associated with atypia among postmenopausal women ( $P < 0.05$ ). The association between atypia and n-3 PUFA, as well as atypia and soy, varied drastically by menopause status (both  $P_{\text{interaction}} = 0.001$ ). A multiple regression model using niacin, n-3 PUFA, and soy intake as predictors (all  $P < 0.01$ ) of atypia status had 94% accuracy for premenopausal participants.

Conclusions: Dietary parameters were much more predictive of breast cancer risk status in premenopausal compared to postmenopausal women. There may be a limited window of opportunity to reduce breast cancer risk by increasing consumption of n-3 PUFA and soy.

## *Introduction*

How does diet influence breast cancer risk? Case-control studies find strong differences between women with and without breast cancer, e.g., higher glycemic load among breast cancer patients (154). Prospective studies also find differences, like an overall lower rate of breast cancer development among those that consume more fruits and vegetables (25). Preclinical studies can demonstrate causality and provide mechanistic explanations; increasing dietary content of n-6 PUFA accelerates mammary carcinogenesis (65) and long-chain n-3 PUFA suppress mammary tumor growth by inhibiting angiogenesis (155). But in controlled human trials, breast cancer risk is not reduced by (a) folate supplementation (156), (b) vitamin E supplementation (157), (c) beta-carotene and vitamin A supplementation (158), (d) combinations of antioxidant supplementation (159, 160), or (e) dietary fat reduction (8). Why have so many randomized dietary interventions failed to prevent breast cancer? It is possible the nutrients studied may not actually influence breast cancer risk. It may also be that the trials were designed at an inappropriate dose or duration. An alternative, unifying theory is that all interventions were tested in middle-aged and older adults, after the chance to influence breast cancer risk through diet had passed.

Early life events, e.g., menarche and first live birth, exert their influence on breast cancer risk decades later (161). The seeds of breast cancer susceptibility may even be planted as early as gestation (162, 163). The younger a woman is when she moves to the U.S., the more her breast cancer risk rises (164, 165); acculturation (including dietary changes) partially mediates the modulation of risk from migration. The protective properties of soy seem strongest when consumed early in a woman's life (166). In brief, timing may be crucial when considering how diet influences breast cancer risk.

To better understand how diet influences breast cancer risk, we measured how the nutrient intake differed between women with and without RPFNA atypia in a sample of high-risk women. To explore time-dependent effects, we tested for different associations between nutrients and atypia status for premenopausal and postmenopausal women.

### *Methods*

#### Participants

Premenopausal and postmenopausal women with an elevated risk of developing breast cancer were recruited from the BCPC at KUMC. The clinic's patients were asked to participate in a cross-sectional study originally designed to investigate the relationship between n-3 PUFA and breast health (Study #1 from above). Participants agreed to complete a survey of diet behavior and have blood sampled by signing an informed consent document approved by our institution's Human Subjects Committee.

#### Breast Cancer Risk and Anthropometrics

Prior to visiting our clinic, information was collected from participants by phone to calculate breast cancer risk using the Gail risk model (120). The Gail risk model is calculated from current age, age of menarche, age at birth of the first child (or nulliparous), family history of breast cancer, number of breast biopsies, finding atypical hyperplasia in a breast biopsy, race, and ethnicity. In the clinic, height and weight were measured.

#### Breast Tissue Analysis

RPFNA was processed as described above.

#### Dietary Assessment

After agreeing to participate, women were asked to complete a paper copy of the original DHQ-I and return it by mail. The DHQ-I is a food frequency questionnaire developed by the National Cancer Institute (NCI). The survey asks about average consumption of >200 foods,

beverages, and nutritional supplements with >400 questions (128). Responses to the multiple-choice questions were entered into Diet\*Calc version 1.4, an online software program developed by the NCI to analyze the DHQ-I. Input was computed into average daily nutrient intake using calculations from the Nutritional Data System for Research (NDS-R) and United States Department of Agriculture (USDA) National Nutrient Database for Standard Reference, release 22. The output units of nutrients and food groups were weight and servings per day, respectively. Other output variables included daily glycemic load, daily energy intake, and the percent energy contribution of macronutrients.

### Statistical Approach

The distribution of all raw output was assessed for normality using the Shapiro-Wilk test and log-transformed as necessary. All nutrients and food groups estimated from the DHQ-I were adjusted for energy intake using the residual method developed by Willett and Stampfer (129). Since the energy-adjusted variables represent relative intake, they were standardized, i.e., converted into Z-scores, to make them comparable with each other.

The association between nutrients and breast cancer risk status (cytology) was measured by logistic regression. Nutrient intake was used as the independent variable with cytology (non-proliferative or hyperplasia without atypia *versus* hyperplasia with atypia) as the dependent variable. Associations between nutrients and atypia were measured separately for premenopausal and postmenopausal participants. An interaction term formally tested whether the association between a nutrient and cytology differed by menopause status. Results are presented as odds ratios of atypia (with 95% confidence interval [CI]) per Z-score increase of nutrient intake. A final model was selected by forward stepwise regression separately for premenopausal and postmenopausal women. The threshold for statistical significance was set to 0.05 without

adjustment for multiple comparisons. *P*-values were calculated by the likelihood-ratio test. JMP version 11.0.0 (SAS Institute) was used for all statistical analyses.

## *Results*

### Sample Characteristics

Between June 2009 and February 2010, 142 women underwent RPFNA at our research clinic, of which 110 met recruitment criteria. Seventy-four women agreed to participate, of which 66 (89%) completed and returned the DHQ-I. One participant was excluded from dietary analysis due to very high alcohol intake: 13 beverages per day. The characteristics of participants included in analyses (N=65) are described in Table 5. Nearly all (n=62) participants self-identified as Caucasian with two reporting Hispanic/Latina ethnicity; others described their race as Asian (n=1), African-American (n=1), or Pacific-Islander (n=1). Seven (11%) women did not attend college; 25 (38%) attended some college or completed a vocational/technical program; 23 (35%) completed a bachelor's degree; and 10 (15%) held a graduate or professional degree. Most (68%) reported an annual household income greater than \$60,000.

Table 5 Selected Characteristics of Women at Elevated Risk of Developing Breast Cancer

	Premenopausal (N=33)	Postmenopausal (N=32)	
	Mean $\pm$ STD or Number (%)		*P
Age (yrs)	42.7 $\pm$ 6.2	55.5 $\pm$ 6.7	<0.0001
Height (cm)	165.4 $\pm$ 6.5	164.1 $\pm$ 5.0	0.31
Weight (kg)	70.0 $\pm$ 12.9	69.6 $\pm$ 12.8	0.92
Body Mass Index (kg/m <sup>2</sup> )	25.5 $\pm$ 4.7	25.8 $\pm$ 5.0	0.93
<sup>a</sup> Family History of Breast Cancer	30 (91%)	29 (91%)	0.97
Age at Menarche (yrs)	12.7 $\pm$ 1.5	12.6 $\pm$ 1.1	0.50
Nulliparous	9 (27%)	4 (13%)	0.12
<sup>b</sup> Age at First Live Birth (yrs)	27.4 $\pm$ 5.7	26.4 $\pm$ 5.3	0.50
Age of Menopause (yrs)	-	44.6 $\pm$ 7.3	-
Use of Oral Contraceptive	28 (85%)	-	-
Use of Hormone Replacement Therapy	-	30 (94%)	-
<sup>c</sup> 5-year Risk of Breast Cancer (%)	2.0 $\pm$ 2.1	3.5 $\pm$ 1.6	<0.0001
Evidence of Cytologic Atypia	12 (36%)	11 (34%)	0.87

\*The *P*-values assessing the difference between groups were calculated by the Mann-Whitney U test or the Pearson's Chi-Squared test for numbers and categories, respectively.

<sup>a</sup>  $\geq 1$  first-degree or  $\geq 2$  second-degree relatives diagnosed with breast cancer before age 60

<sup>b</sup> Calculated among parous women

<sup>c</sup> Calculated by the Gail Risk Assessment Tool(120). In the United States, the average risk of developing breast cancer is 0.8% for a 43yr old, 1.2% for a 48yr old, and 1.5% for a 56yr old Caucasian woman

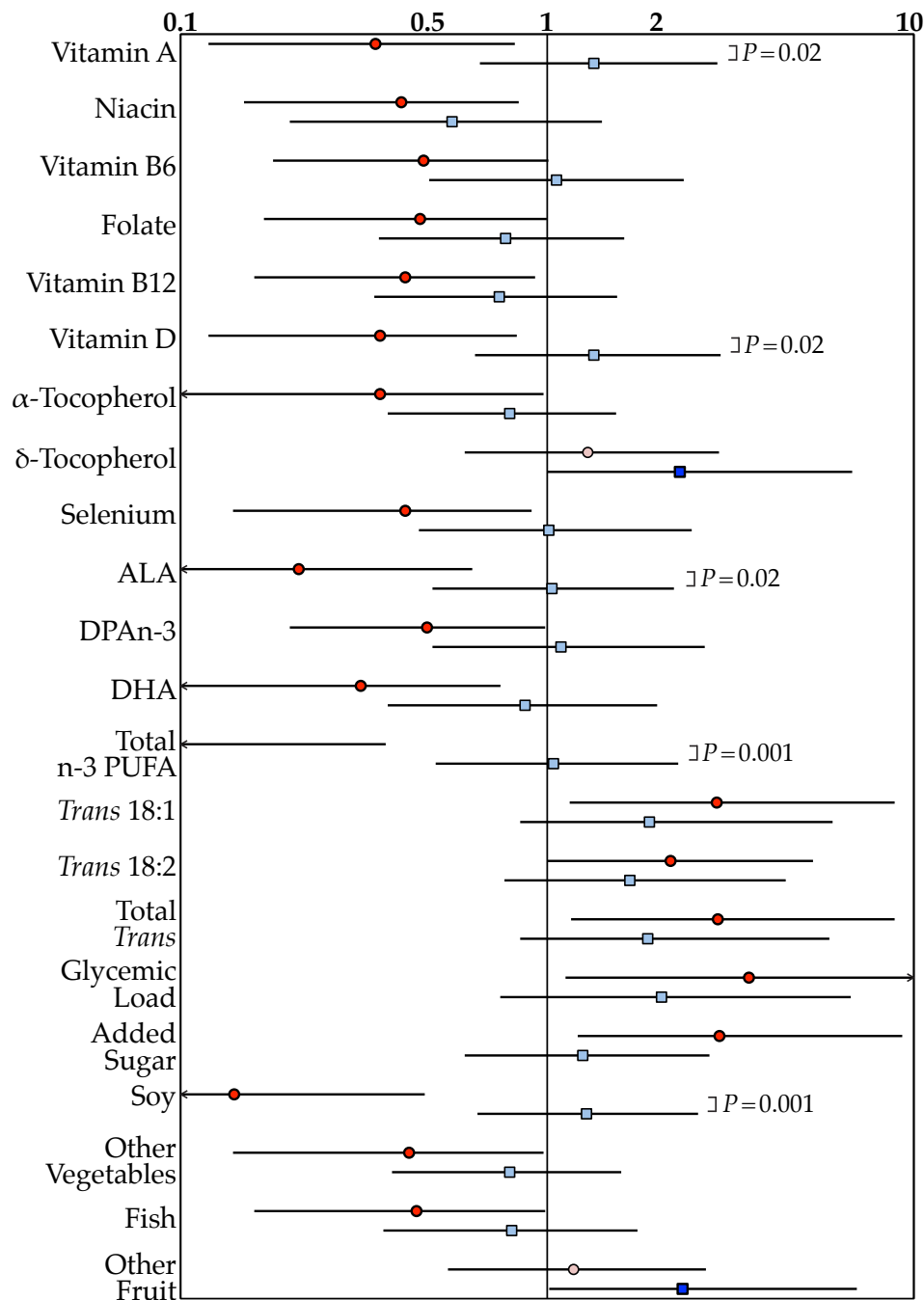
Age of participants ranged from 25 to 65 years. Due to surgically induced menopause (oophorectomy) postmenopausal women were as young as 41. Nevertheless, postmenopausal women were older and, because breast cancer risk rises with age, had a higher estimated risk of developing breast cancer compared to premenopausal women. Overall, participants had an estimated breast cancer risk greater than twice the average for the general population. The prevalence of cytologic atypia was equal between premenopausal and postmenopausal women. The youngest woman with atypia was 35; the oldest was 65.

## Diet Analysis

Among premenopausal women, greater consumption of niacin, pyridoxine, folate, vitamin B12, vitamin D,  $\alpha$ -tocopherol, selenium, n-3 PUFA, “other vegetables,” fish, and soy predicted a lower likelihood of atypia, while higher glycemic load and intake of added sugar, and trans fat was associated with evidence of atypia (Figure 6). Higher intakes  $\delta$ -tocopherol and “other fruit” were associated with atypia among postmenopausal women ( $P<0.05$ ).

The significant interactions indicated in Figure 6 indicate that the odds ratios were different for the two cohorts. Notably, there were strong interactions with menopause for n-3 PUFA and soy (both  $P_{\text{interaction}}=0.001$ ). Total n-3 PUFA intake was inversely associated with atypia among premenopausal ( $P<0.0001$ ), but not postmenopausal women ( $P=0.91$ ). Similarly, soy intake was associated with lower likelihood of atypia for premenopausal ( $P=0.0003$ ) and not for postmenopausal women ( $P=0.48$ ). The menopause-specific associations were not due to overall differences in intake between premenopausal and postmenopausal participants (Table 6).

Stepwise regression determined a final model for premenopausal participants that included niacin ( $P=0.003$ ), total n-3 PUFA ( $P=0.002$ ), and soy ( $P=0.006$ ) as significant predictors of atypia. The model had 92% sensitivity and 95% specificity; 21 of the 23 women with atypia were predicted to have atypia by the model and 40 of 42 women without atypia were correctly identified as probably not having atypia. For postmenopausal participants, higher intake of  $\delta$ -tocopherol ( $P=0.03$ ) and “other fruit” ( $p=0.03$ ) were independently associated with a higher likelihood of atypia; this model had lower sensitivity (55%) than specificity (90%), i.e., it could more accurately predict which postmenopausal women did not have atypia compared to identifying those with atypia.



**Figure 6: Associations between Nutrients and RPFNA Atypia by Menopause Status.**

Red circles are the odds ratio (OR) for exhibiting cytologic atypia per standard deviation (Z-score) increase in consumption for premenopausal participants; the blue squares are the OR for postmenopausal participants. Colors are darkened for significant associations ( $P < 0.05$ ). The error bars represent the 95% confidence interval. Significant interactions with menopause status are indicated as  $P$ -values in the figure; a low  $P$ -value indicates that the association between the nutrient/food group and atypia is different for premenopausal compared to postmenopausal women. The “Other Vegetables” U.S.D.A. food group is comprised of string bean, cabbage, cauliflower, brussel sprout, and lettuce. The “Other Fruit” U.S.D.A. food group is mostly comprised of grape, apple, pear, peach, nectarine, plum, banana, apricot, and all products thereof, e.g. juice, jelly, and pies.



Table 6 Estimated Daily Intake using the Diet History Questionnaire I

	Premenopausal (N=33)	Postmenopausal (N=32)	
	Mean ± STD		<i>P</i> <sup>a</sup>
Vitamin A (RAE mcg)	642 ± 288	690. ± 385	0.38
Niacin (B3) (mg)	17.6 ± 6.8	19.5 ± 6.7	0.48
Pyridoxine (B6) (mg)	1.56 ± 0.62	1.62 ± 0.67	0.32
Folate (mcg)	308 ± 120	327 ± 129	0.68
Vitamin B12 (mcg)	3.25 ± 1.49	3.66 ± 1.62	0.50
Vitamin D (mcg <sup>b</sup> )	3.24 ± 2.18	3.69 ± 2.61	0.88
α-Tocopherol (mg)	7.22 ± 3.65	8.85 ± 3.98	0.24
δ-Tocopherol (mg)	1.36 ± 0.48	1.58 ± 0.63	0.20
Selenium (mcg)	71.0 ± 28.5	75.7 ± 26.3	0.55
ALA [18:3n3] (mg)	894 ± 374	1039 ± 448	0.22
DPAn-3 [22:5n3] (mg)	10. ± 10.	13 ± 8	0.07
DHA [22:6n3] (mg)	84 ± 96	95 ± 68	0.12
Total n-3 PUFA (g)	1.07 ± 0.53	1.24 ± 0.50	0.17
<i>Trans</i> 18:1 (g)	2.12 ± 0.83	2.42 ± 1.03	0.30
<i>Trans</i> 18:2 (mg)	290 ± 105	324 ± 124	0.46
Total <i>Trans</i> Fat (g)	2.47 ± 0.94	2.81 ± 1.17	0.31
Glycemic Load <sup>c</sup>	76.9 ± 28.0	81.5 ± 28.6	0.30
Added Sugar (g)	38.9 ± 23.6	46.0 ± 26.1	0.48
Soy (oz)	0.118 ± 0.222	0.155 ± 0.248	0.31
Other Vegetables (cup)	1.66 ± 1.48	1.74 ± 1.38	0.85
Fish (oz)	0.43 ± 0.74	0.45 ± 0.38	0.07
Other Fruit (cup)	1.11 ± 0.94	1.14 ± 1.03	0.75

<sup>a</sup> The *P*-value assesses the difference in intake between premenopausal and postmenopausal women using the Mann-Whitney U test after adjustment for energy intake. With all *P*-values greater than 0.05, there is no evidence that premenopausal and postmenopausal women differed in their diet overall.

<sup>b</sup> One microgram of Vitamin D is equivalent to 40 international units (IU).

<sup>c</sup> The glycemic load is calculated as the sum of products of glycemic index multiplied by the number of grams of digestible carbohydrate of each carbohydrate-containing food or drink. RAE = retinol activity equivalents, ALA = alpha-linolenic acid, EPA = eicosapentaenoic acid, DHA = docosahexaenoic acid, PUFA = polyunsaturated fatty acids.

### *Discussion*

The associations between diet and breast cancer risk status that we identified (19 for premenopausal women, 2 for postmenopausal) have mechanistic and epidemiologic support. And when available, evidence for time-dependent effects are noted below.

A pooled analysis of seven thousand women followed for a median of 4.3 years found that those with higher serum levels of  $\alpha$ -carotene and  $\beta$ -carotene (precursors of Vitamin A) were less likely to develop breast cancer, especially estrogen-receptor negative (ER-) tumors (167). ER- breast cancer is more common among younger, premenopausal versus older, postmenopausal women (168). Vitamin A intake was correlated with consumption of the “other vegetable” food group ( $r=0.43$ ). The higher short-term risk among premenopausal participants with low intake of vitamin A and “other vegetables” in our study supports the hypothesis that eating carotenoid-rich vegetables may protect against breast cancer.

Epidemiologic studies of breast cancer risk provide mixed results for B-vitamins. For niacin, two prospective studies did not find evidence of an association between estimated intake and breast cancer risk (169, 170). Higher serum levels of pyridoxal 5'-phosphate (vitamin B6) tend to be associated with lower breast cancer risk (171). For folate intake, a meta-analysis of prospective studies found a J-shaped relationship for breast cancer risk, with moderate levels conferring protection but higher consumption significantly increasing risk (172); natural versus synthetic folate may underlie this curious association (173). Vitamin B12 levels in serum are not consistently associated with a lower breast cancer risk (171). Our finding of an inverse association between atypia and niacin, B6, folate, and B12 warrant more investigation into the relationships between B-vitamin consumption and breast cancer risk with attention to effects dependent on source, dose, and timing.

There are several plausible mechanisms by which B-vitamins may protect against breast cancer development. Niacin is not only a cofactor for DNA repair, but it also regulates response to calorie restriction (174, 175); calorie restriction protects against mammary tumorigenesis in preclinical models (176) and might in humans (177). Additionally, a niacin-activated receptor was recently characterized as a mammary tumor suppressor gene (178). Pyridoxine, folate, and vitamin B12 participate in the methyl-cycle, which exerts widespread epigenetic effects by modulating DNA and histone methylation (179). In a preclinical study, methyl donor supplementation during puberty decreased the rate of mammary tumorigenesis in adulthood (180). In summary, B-vitamin consumption may dampen breast cancer risk via their multitudinous effects on gene expression.

The association between vitamin D and breast cancer remains an active area of research (181-185). In contrast to our findings, a meta-analysis concluded that higher serum vitamin D was associated with lower risk in postmenopausal, but not among premenopausal women (181); another found a consistent protective association regardless of menopause status (183). The effect of vitamin D on breast cancer risk has been reported to interact with mammographic density (182), genetic polymorphisms (185), or racial/ethnic identity (184). Lastly, the effect on breast cancer risk from vitamin D *per se* may be difficult to statistically isolate, because of its strong colinearity with several known behavioral risk factors for breast cancer: body mass index, smoking, and physical activity (186). Our observed low intake of vitamin D among premenopausal with cytologic atypia warrants further investigation into the vitamin D-breast cancer link.

Vitamin E encompasses a class of lipophilic nutrients with antioxidant properties (187, 188). The variety of tocopherols and tocotrienols differ in structure and food source (187, 188); the DHQ-I only estimated intake of four. The inverse association between cytologic atypia and

$\alpha$ -tocopherol intake among premenopausal women is congruent with early epidemiologic patterns of protection that motivated the conduction of randomized, controlled supplementation trials, which did not prevent cardiovascular disease or cancer (157, 189). In this study,  $\alpha$ -tocopherol intake may be a proxy for eating more nutritious foods, because intake correlated with “other vegetable” consumption ( $r=0.40$ ). Given the anti-proliferative, anti-inflammatory, and antioxidant effects of  $\delta$ -tocopherol (measured *in vitro* and *in vivo*) (187, 188), the positive association between delta-tocopherol intake and atypia among postmenopausal women is surprising. This counterintuitive observation may reflect the foods that most contribute to  $\delta$ -tocopherol intake are margarine, corn bread/muffins, and baked desserts (190); there was a strong correlation between  $\delta$ -tocopherol and total *trans* fat consumption ( $r=0.76$ ). Interestingly, higher plasma  $\delta$ -tocopherol concentration has been linked to greater colon cancer risk (191). The associations for Vitamin E isomers ( $\alpha$ - and  $\delta$ -tocopherol) we observed prompt a more detailed analysis of how the intake of their principal food sources influence breast cancer risk.

We found an inverse association between selenium intake and likelihood of atypia among premenopausal women; this is consistent with a meta-analysis that found lower levels of this essential micronutrient in serum is associated with higher breast cancer risk (192).

Many others have suggested greater consumption of n-3 PUFA might protect against breast cancer development (52, 64, 193, 194). The anti-carcinogenic mechanisms of n-3 PUFA are reviewed in detail elsewhere (195). The strong interaction with menopause status that we measured adds nuance to the literature in that it suggests consuming more n-3 PUFA may be more protective against breast cancer when consumed earlier rather later in adulthood.

Soy has been extensively studied as a dietary modifier of breast cancer risk, because it contains isoflavones, which carry mild estrogenic and anti-estrogenic effects (196). Premenopausal women have higher endogenous estrogen; therefore, it has been hypothesized

that soy exerts its protective effects against breast cancer earlier in life partially by interfering with estrogen signaling (166). Preclinical work has shown early exposure to genistein, the main soy isoflavone, promotes mammary gland differentiation, which decreases susceptibility for later mammary tumor development (197). Although we did not directly measure prepubertal diet, we did find a protective association for soy among the younger, premenopausal women in our sample.

Greater consumption of *trans* fatty acids increased the odds of RPFNA atypia. Epidemiologists report breast cancer risk is positively associated with higher levels of *trans* fatty acids in serum (141) and adipose tissue (198). Reducing consumption of foods rich in industrially produced *trans* fatty acids merits exploration as an intervention to lower breast cancer risk.

Our study is more exploratory than conclusive, with our results meant to generate hypotheses rather than test them. The smaller sample size decreased power to detect differences, but also indicated stronger effect sizes for significant associations. The major limitation of this study is its increased chance of type I error from performing multiple statistical tests. Although we attempted to control for that by multiple regression modeling, the final models should be interpreted with caution, because they are likely biased to our sample (199). Lastly, given that n-3 PUFA and soy are considered health promoting in the general public, a higher intake may only reflect a more health-conscious lifestyle that actually drives the observed associations with premenopausal atypia in this high-risk sample of women.

In summary, carcinogenesis is a prolonged process and the dietary contribution to breast cancer risk may hinge on timing. We found that the nutrient density of a woman's diet was much more predictive of short-term risk status in premenopausal women compared to postmenopausal women. The directions of the associations reported for B-vitamins, n-3 PUFA, soy, and trans fat

are consistent with previous reports. The weak associations for postmenopausal participants merit further elucidation. Dietary intervention trials for primary prevention of breast cancer could be more effective if initiated at an earlier rather than later age, because there may be a limited window of opportunity to modify breast cancer risk through diet.

## **Chapter Five:**

# **Using Tissue Fatty Acids to Validate an Empirically-Derived Modern-Traditional Dietary Pattern that Predicts Short-Term Breast Cancer Risk Status**

## *Abstract*

Background: Despite scores of studies relating nutrition to risk of developing breast cancer, there is no clear dietary pattern for risk reduction.

Objective: The purpose of this analysis was to empirically define and tissue-validate a dietary pattern that predicts cytologic atypia, a biomarker of short-term breast cancer risk.

Methods: Breast tissue was obtained by RPFNA from 65 women at elevated risk and assessed for cytology. We analyzed the fatty acid compositions of breast adipose and three lipid compartments in blood. Dietary behavior was measured by the National Cancer Institute's food frequency questionnaire. Dietary variables (n=131) were computed into dietary patterns by principal components analysis. The associations between dietary patterns and (a) tissue fatty acids and (b) atypia were respectively assessed by Spearman's correlation and logistic regression.

Results: A dietary pattern representing a Modern-Traditional dietary continuum was identified, with positive scores indicating a more Traditional diet of vegetables, fish, and poultry, and negative scores reflecting a more Modern diet of grains, added sugar, trans fat, and dairy. A more Traditional dietary pattern positively correlated with levels of long-chain n-3 PUFA in blood and negatively correlated with both n-6 PUFA and industrially produced trans fatty acids in blood and adipose (all  $P < 0.05$ ). Each standard deviation increase in Modern-Traditional dietary pattern score was associated with 50% lower odds of atypia (95% CI: 0.26 to 0.88), with a stronger effect among younger participants (interaction for age  $P = 0.05$ ).

Conclusions: This is the first report of a dietary pattern substantiated by tissue fat content. A more Traditional, less Modern dietary pattern was associated with a lower short-term risk of breast cancer among younger women. A dietary intervention that replaces modern foods (grains,



added sugar, and dairy) with vegetables, fish, and poultry should be explored for breast cancer prevention.

## *Introduction*

Heredity, lifestyle, time, and chance interact to determine whether (and when) someone develops breast cancer. Behavior, not genetics, explains the majority of the variation in breast cancer risk (200). Diet is an important health behavior (201), but among all dietary habits, there is only consensus that a higher alcohol intake increases breast cancer risk (202).

Most studies of dietary contribution to breast cancer risk have used a reductionist approach, analyzing the association between quantiles of nutrient intake (203) and food groups (25, 204) after statistically-adjusting for (up to 17) confounders (205). This paradigm searches for dietary differences that can be straightforwardly tested by randomized, controlled trials. The only randomized dietary interventions for primary prevention of breast cancer did not significantly lower the rate of breast cancer by reducing dietary fat intake (7, 8). The unexpected results may be due to the complexity of diet. Targeting an entire macronutrient class may have been ineffective because different types of fat have different effects on breast cancer risk. N-3 polyunsaturated fatty acids (PUFA) and monounsaturated fatty acids are generally protective (64, 206), while higher n-6 PUFA and trans fat consumption is associated with higher risk (65, 206).

As an alternative approach to focusing on nutrients, dietary patterns can account for complex interactions among dietary constituents (82). Dietary patterns can be created from a dataset by multivariate statistical methods (110, 112). However, this methodology is beset by (a) ambiguous interpretation of the meaning of the dietary patterns and (b) difficulty replicating results and generalizing to other populations. This study strives to address these shortcomings of dietary pattern research by reifying a dietary pattern with biomarkers of dietary behavior, namely tissue fatty acids. In this analysis, we identified dietary patterns, correlated them with tissue fatty acids, and measured the associations between dietary patterns and a validated biomarker of breast cancer risk, cytologic atypia obtained by RPFNA.

## *Subjects and Methods*

### Participants

Premenopausal and postmenopausal women at an elevated risk of developing breast cancer were eligible for RPFNA at our research clinic. Elevated risk was based on one or more of the following criteria: (a) at least one first-degree relative that was diagnosed with breast cancer before age 60, (b) at least two second-degree relatives similarly affected, (c) at least one prior breast biopsy diagnosed as atypical hyperplasia or ductal/lobular carcinoma in situ, (d) multiple biopsies from suspicious mammograms, or (e)  $\geq 50\%$  mammographic density.

Participants signed an informed consent document approved by the University of Kansas Medical Center Human Subjects Committee, which is responsible for institutional ethical standards.

### Breast Cancer Risk and Anthropometrics

Information needed to calculate breast cancer risk using the Gail risk model (120) was collected from participants by phone prior to visiting our clinic. The Gail risk model is calculated from current age, age of menarche, age at the time of the birth of the first child (or nulliparous), family history of breast cancer, number of breast biopsies, number of breast biopsies showing atypical hyperplasia, race, and ethnicity. Height was measured by a standing stadiometer without shoes on to the nearest millimeter. Weight was measured by an electronic scale to the nearest 100g.

### Dietary Assessment

Participants completed the DHQ-I (128). Responses to the multiple-choice questions were entered into Diet\*Calc version 1.4, a software program developed by the NCI to analyze the DHQ-I. Input was computed into to average daily nutrient intake using calculations from the Nutritional Data System for Research (NDS-R) and United States Department of Agriculture

(USDA) National Nutrient Database for Standard Reference, release 22. The output of most dietary parameters (123 of 131) was as weight or servings per day. Other variables included glycemic load, total energy intake, the percent energy contribution of carbohydrates, fat (with subtypes), and protein.

#### Analysis of Tissue Fatty Acids

Details of tissue harvest by RPFNA, storage, processing, and fatty acid analysis are described above. Briefly, a blinded cytopathologist rated specimens as nonproliferative, hyperplasia without atypia, hyperplasia with atypia, or possible malignancy. Blood was separated into plasma and erythrocytes. Phospholipids and triacylglycerides were isolated from plasma and breast tissue (RPFNA). The fatty acid composition of phospholipids from erythrocytes were also measured. After isolation and transmethylation, fatty acid methyl ester products were analyzed by a Varian 3900 gas chromatogram (Agilent Technologies, Santa Clara, California). Fatty acid composition was calculated as weight percent using a standard mixture.

#### Statistical Analyses

##### *Measuring Dietary Patterns by Principal Components Analysis*

Principal components analysis (PCA) was performed on the correlation matrix of dietary parameters, e.g., kilocalories, macronutrients, micronutrients, food groups, glycemic load, alcohol, and proportion of energy from macronutrients. PCA is a multivariate technique that consolidates correlated continuous variables into fewer, uncorrelated factors that reveal the internal structure of the data. The number of factors to retain for analysis was decided by the Scree test, which uses visual inspection to select the cut-point whereat small differences in eigenvalues begin. A recent methods report found a 3-component solution for PCA of diet identified by the Scree test to be most reproducible (130).

### *Biomarker Validation of Dietary Patterns*

Biological evidence of fat consumption within dietary patterns was measured by correlating the dietary patterns with fatty acids in tissue samples. The associations were measured using Spearman's rank correlation coefficient to account for non-normal distributions. Different lipid compartments indicate fat intake over different lengths of time; plasma triacylglycerides reflect fat intake over the previous hours to days, plasma phospholipids days to weeks, erythrocyte phospholipids weeks to months, and breast triacylglycerides months to years (125).

### *Dietary Pattern Associations with RPFNA atypia*

The PCA-derived dietary patterns were tested for an association with atypia by simple logistic regression. Dietary patterns were tested for an interaction with menopause status, age, and body mass index ( $\text{kg}/\text{m}^2$  [BMI]). *P*-values for interactions are presented along with results from stratified analyses by menopause status, above/below median age (49 or younger versus 50 and older), and above/below median BMI (normal [less than  $25 \text{ kg}/\text{m}^2$ ] versus overweight or obese [at least  $25 \text{ kg}/\text{m}^2$ ]).

### *Statistical Summary*

The acceptable false positive rate for each two-sided test was set at 5% ( $\alpha=0.05$ ). Adjustments were not made for multiple comparisons. All analyses were performed with JMP version 11.0.0 (SAS Institute Inc., Cary, NC, USA).

## *Results*

### Sample Characteristics

Sixty-six women completed and returned the DHQ-I and had RPFNA assessed for atypia status. One participant was excluded from analysis for an extremely high intake of alcohol: a reported 13 beverages per day. The remaining participants' demographics, reproductive history,

and anthropometrics are listed in Table 9. Women with atypia were taller than women without atypia; each centimeter in height increased the odds of atypia by 15% (OR 95% CI: 1.05 to 1.28).

<i>Table 7 Participant Characteristics</i>		
	<u>Atypia (n=23)</u>	<u>No Atypia (n=42)</u>
	Mean±STD (Range) or Number (%)	
Age (yrs)	49±8.8 (35-65)	49±9.3 (25-64)
Premenopausal (vs Postmenopausal)	12 (52%)	21 (50%)
Oral Contraceptives <sup>a</sup>	9/12 (75%)	19/21 (90%)
Hormone Replacement Therapy <sup>b</sup>	11/11 (100%)	19/21 (90%)
Positive Family History <sup>c</sup>	22 (96%)	37 (88%)
Age at Menarche (yrs)	12.6±0.9 (11-14)	12.7±1.5 (9-16)
Age at First Live Birth (yrs)	26.4±4.5 (17-34)	27.1±6.0 (17-37)
Number of Live Births	1.9±1.1 (0-4)	1.9±1.2 (0-4)
5yr Gail Risk <sup>d</sup>	2.9±2.6% (0.84-12.7%)	2.6±1.7% (0.04-7.5%)
Height (cm)	168±6.0 (157-180)	163±5.2 (154-175)
Weight (Kg)	72.5±13.9 (52-102)	68.3±12.0 (46-109)
Body Mass Index (Kg/m <sup>2</sup> )	25.8±5.1 (20-38)	25.6±4.7 (17-44)

<sup>a</sup> Portion calculated among premenopausal women within each group.

<sup>b</sup> Portion calculated among postmenopausal women within each group.

<sup>c</sup> At least one first-degree relative or at least two second-degree relatives diagnosed with breast cancer before age 60.

<sup>d</sup> Individual projected likelihood of breast cancer incidence over the next five years using the Gail risk model (120). For reference, the average risk for a 49 yr old woman is 1.2%.

### Identification of Dietary Patterns by Principal Component Analysis

Carbohydrates were the richest source of energy (mean $\pm$ STD, 49 $\pm$ 9.2%), followed by fat (33 $\pm$ 7.0%), protein (17 $\pm$ 2.5%), and alcohol (3.4 $\pm$ 5.6%) (Figure 7). The intake of USDA food groups by women with and without atypia is shown in Figure 8.

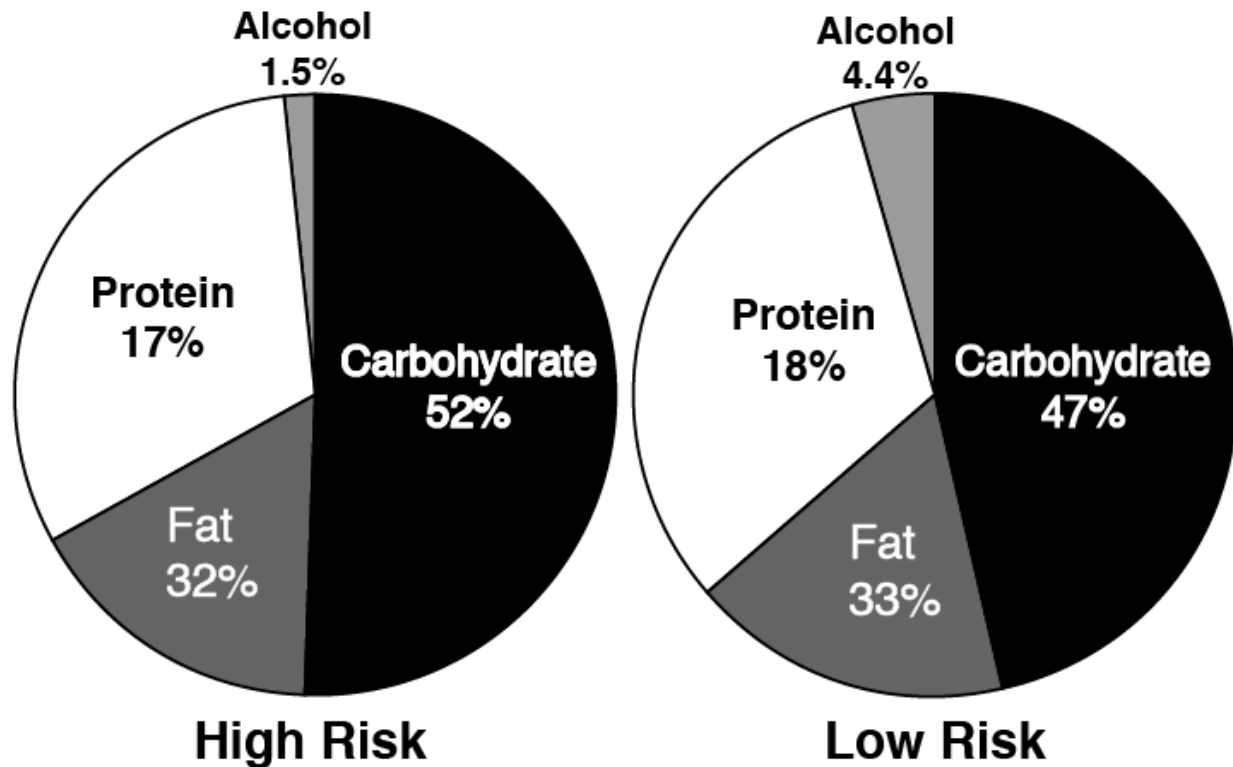
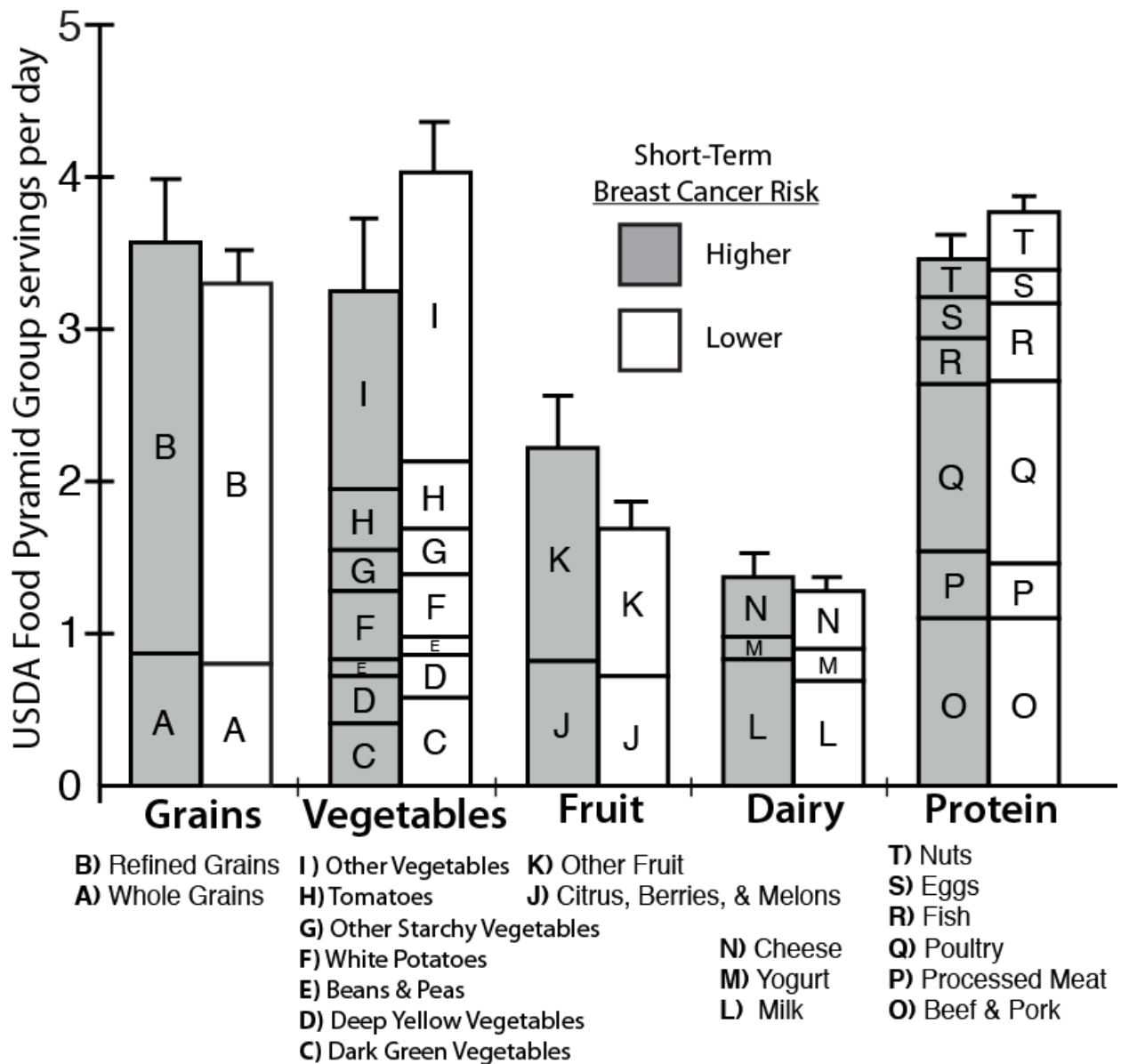


Figure 7: **Average Estimated Macronutrient Energy Proportion.** The average macronutrient energy distribution is shown for the 23 women with higher short-term risk of breast cancer (“High Risk”) and the 42 women without evidence of RPFNA atypia (“Low Risk”).

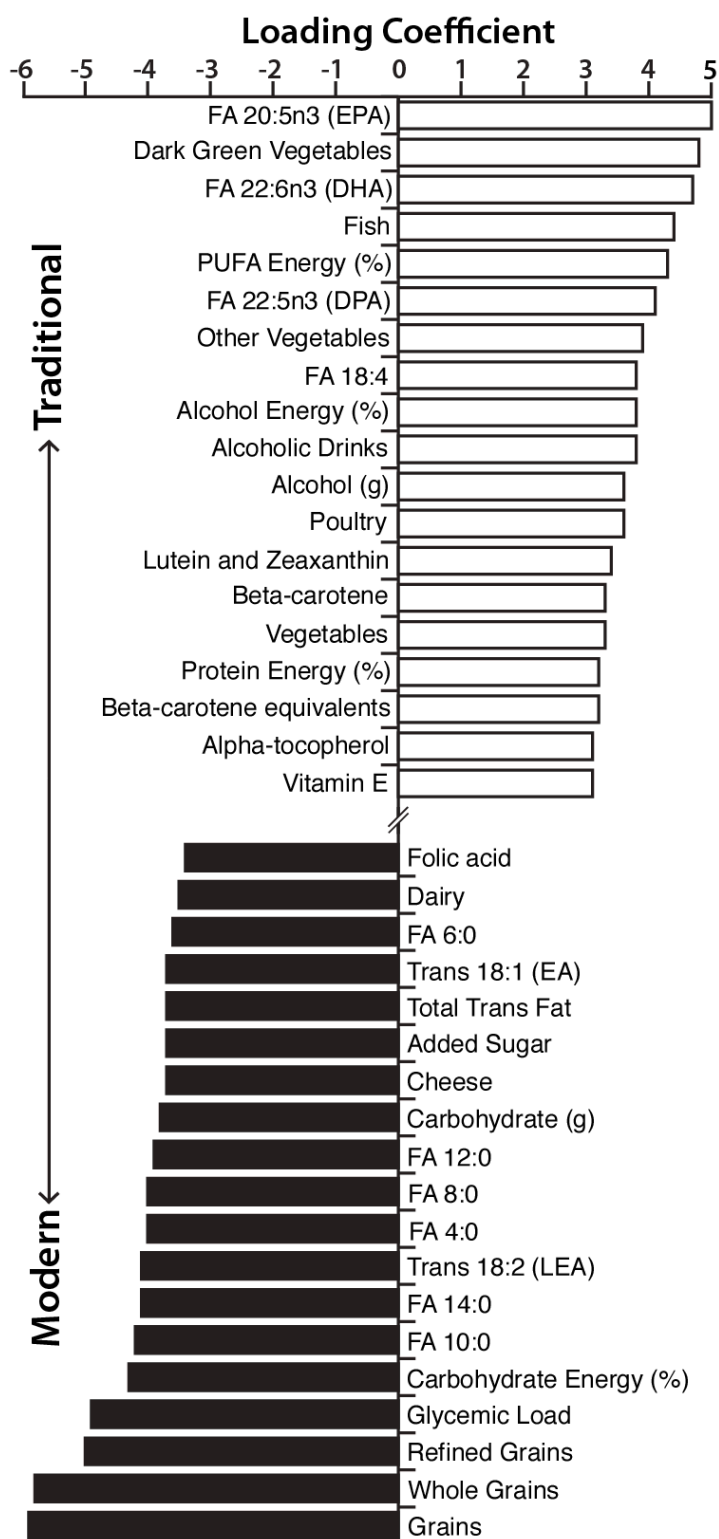


**Figure 8: Daily Consumption of 20 USDA Pyramid Food Groups.** The average daily consumption of USDA Pyramid Food Groups estimated by the NCI's food frequency questionnaire are shown. Error bars represent standard error of the mean. Women with higher short-term risk of breast cancer (grey) exhibited cytologic atypia by RPFNA (n=23). White bars represent women without evidence of RPFNA atypia (n=42).

Surprisingly, neither height ( $r=-0.05$ ), nor weight ( $r=-0.03$ ), nor body mass index ( $r=-0.02$ ) correlated with estimated daily calorie consumption. Summary statistics of raw output of USDA food groups are available in Supplemental Table 9 and actual items from the DHQ-I that contribute to USDA food group servings are available in Supplemental Table 10.



Three dietary patterns were retained by Scree plot inspection. The first dietary pattern explained 41% of the variance and positively loaded with nearly all variables; it was named “Energy” because it near-perfectly correlated with daily energy intake ( $r=0.95$ ). The second dietary pattern explained 14% of the variance; it was named the “High-Fat-Meat-Low-Carb” pattern (207), because it loaded positively with meat, alcohol, and fat-related variables and negatively with dairy, fruit, and total carbohydrates (Supplemental Table 11). The High-Fat-Meat-Low-Carb pattern was positively correlated with % energy from fat ( $r=0.83$ ), negatively with carbohydrates ( $r=-0.79$ ). The third principal component explained 7% of the variance and was named the “Modern-Traditional” dietary pattern, because a higher score indicated a greater intake of vegetables, fish, alcohol, and chicken and a lower score indicated a greater intake of grains, added sugar, trans fat, and dairy (Figure 9). Positive scores represented a more Traditional diet, negative scores a Modern diet.



**Figure 9: Modern-Traditional Dietary Pattern Score Calculation.**

The Modern-Traditional diet score is the sum of each dietary parameter's z-score multiplied by its loading coefficient, which is represented as the bars (10x). Black bars indicate negative loading, i.e., a greater intake contributes to a more negative score, and vice versa for white bars. Negative scores represent a more Modern diet, positive scores a more Traditional diet. FA = fatty acid, LEA = linolelaidic acid, EA = elaidic acid, DPA = (n-3) docosapentaenoic acid, DHA = docosahexaenoic acid, EPA = eicosapentaenoic acid.

Income, weight, BMI, and height did not correlate with any dietary pattern ( $P>0.19$ ). Age was unrelated to Energy and High-Fat-Meat-Low-Carb ( $P>0.47$ ); interestingly, older women reported a more Traditional and younger women a more Modern diet ( $r=0.27$ ,  $P=0.03$ ).

#### Tissue Validation of Dietary Patterns

The concentration of fatty acids in plasma phospholipids, plasma triacylglycerides, red blood cell phospholipids, and breast triacylglycerides are available in Landscape Supplemental Table 12. Energy was negatively correlated with linoleic acid in plasma triacylglycerides ( $r=-0.25$ ,  $P=0.05$ ), elaidic acid in breast triacylglycerides ( $r=-0.36$ ,  $P=0.04$ ), and alpha-linolenic acid in breast triacylglycerides ( $r=-0.36$ ,  $P=0.04$ ). The High-Fat-Meat-Low-Carb pattern was not significantly correlated with any tissue fatty acid ( $P>0.07$ ). The correlations between the Modern-Traditional dietary pattern and concentrations of fatty acids in tissue are presented in Table 8. A more Traditional, less Modern dietary pattern was significantly associated with (a) higher oleic acid, (b) higher eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), (c) lower linoleic acid, and (d) lower elaidic acid and linolelaidic acid. Women with a higher Modern-Traditional dietary pattern score tended to have a higher total n-3:n-6 PUFA ratio in their red blood cells ( $r=0.33$ ,  $P=0.01$ ).

Table 8 Modern-Traditional Score Correlations with Tissue Fatty Acids

Class	Fatty Acid	Tissue Lipid Compartment			
		Plasma Phospholipids	Plasma Triacylglycerides	Erythrocyte Phospholipids	Breast Adipose Triacylglycerides
Mono	Oleic (18:1n9c)	0.24	0.45***	0.12	-0.05
	Alpha-Linolenic (18:3n3)	0.13	-0.21	0.03	-0.13
N-3 PUFA	Eicosapentaenoic (20:5n3)	0.41**	0.13	0.35**	0.02
	Docosahexaenoic (22:6n3)	0.22	0.30*	0.33**	0.11
N-6 PUFA	Linoleic (18:2n6c)	0.04	-0.28*	0.06	-0.40*
	Arachidonic (20:4n6)	0.01	-0.02	0.18	0.04
<i>Trans</i>	Elaidic (18:1n9t)	-0.29*	-0.22	-0.36**	-0.16
	Linolelaidic (18:2n6t)	-0.16	-0.25*	-0.32*	-0.41*

Spearman's correlations are shown. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ . Abbreviations: Mono = monounsaturated fatty acids, PUFA = polyunsaturated fatty acids. *Trans* = industrial trans fatty acids.

#### Associations between RPFNA Atypia and Dietary Patterns

All associations, interactions, and stratified analyses of the three identified dietary patterns are presented in Supplemental Table 13. The Energy dietary pattern exhibited no significant associations or interactions with atypia. The High-Fat-Meat-Low-Carb dietary pattern was not associated with atypia overall. However, there was a significant interaction with BMI ( $P_{\text{interaction}} = 0.02$ ); odds of atypia increased for higher scores at elevated BMI, but decreased at lower BMI. Among the entire sample, a more Traditional dietary pattern score was associated with a lower likelihood of atypia (Figure 10); the odds ratio per standard deviation increase was 0.50 (95% CI: 0.26 to 0.88). The association between the Modern-Traditional diet varied by age ( $P_{\text{interaction}} = 0.05$ ); a more Traditional diet was strongly associated with a lower likelihood of atypia among women 49 and younger ( $P = 0.003$ ), but not among older women ( $P = 0.83$ ).

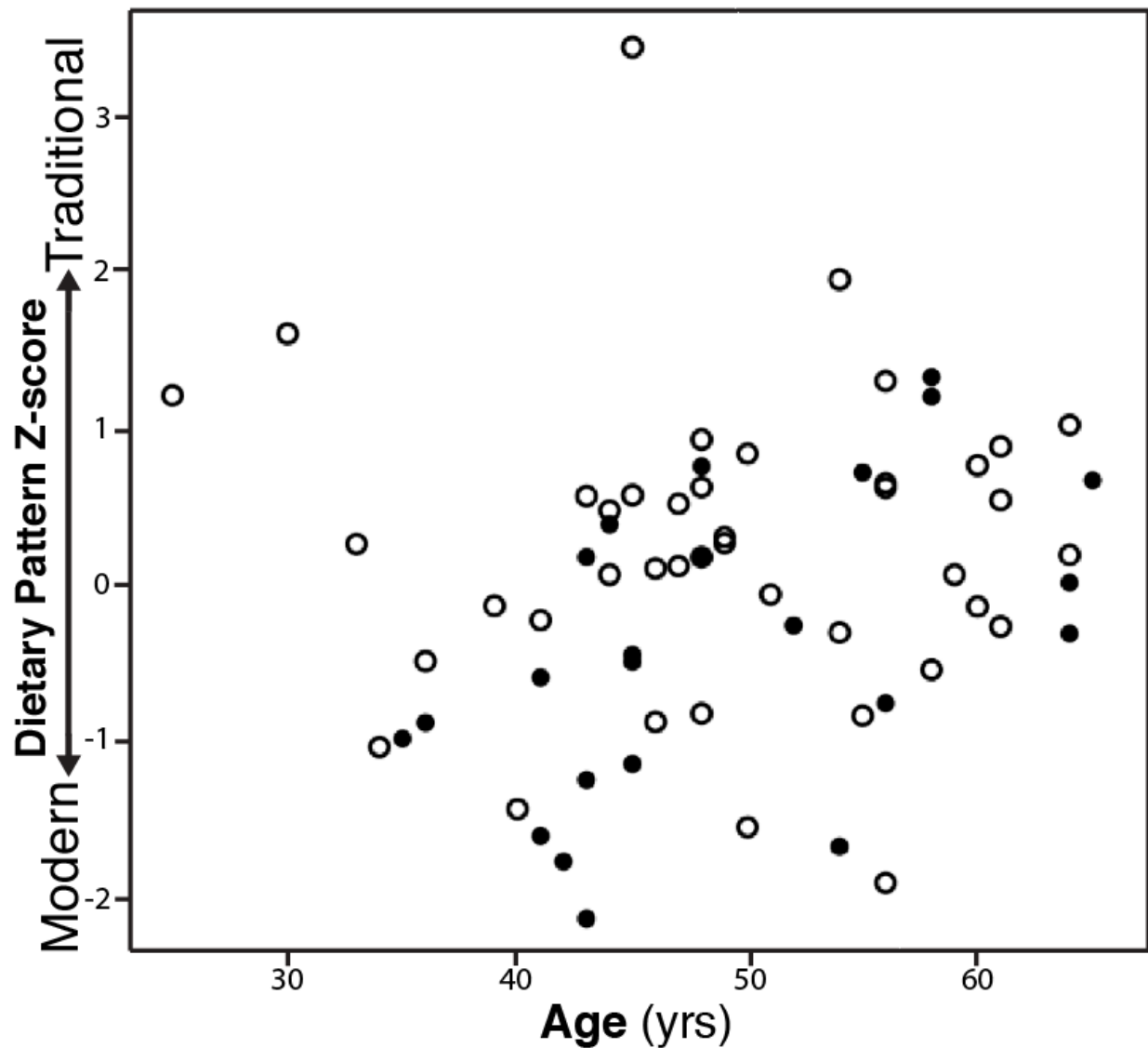


Figure 10: **Association between a Modern-Traditional Dietary Pattern and RPFNA Atypia by Age.** The black circles represent women with cytologic atypia, and the white circles represent women without. A more Modern diet (lower score) was associated with atypia, overall; this association was stronger among younger women.

## *Discussion*

To our knowledge, this is the first report to validate a multivariate-derived dietary pattern with tissue fatty acid composition. The positive correlation between a Traditional dietary pattern and levels of oleic acid in plasma triacylglycerides could reflect recent consumption of olive oil or canola (rapeseed) oil (208). The Traditional dietary pattern's high loading of fish intake was confirmed by the positive correlations with concentrations of long-chain n-3 PUFA, EPA and DHA, in circulating phospholipids. At the opposite end, a more Modern diet was directly associated with tissue levels of industrially-produced trans fats, elaidic and linolelaidic acids (209). The correlation between a Modern dietary pattern and tissue linoleic acid indicates stronger adherence to a Westernized diet, which is characterized by a high n-6 PUFA intake as linoleic acid (210). Overall, these associations with tissue fat show that a more Traditional dietary pattern indicates eating more monounsaturated fat and n-3 PUFA, while a Modern diet is characterized by greater consumption of industrially-produced trans fat, and n-6 PUFA.

The negative correlations between the Energy dietary pattern and linoleic, elaidic, and alpha-linolenic acids were weak. However, these associations could indicate a diet with little diversity, low physical activity, and/or hasty completion of the questionnaire.

Taller women in our sample tended to have atypia, which is consistent with epidemiologic reports that height is an independent risk factor for breast cancer (211). Adult height is partially determined by childhood environment, especially nutrition (212); therefore, dietary effects on breast cancer risk may begin early in life (213). A model depicting the relationships among atypia, height, and Modern-Traditional diet in our sample is shown in Figure 11.

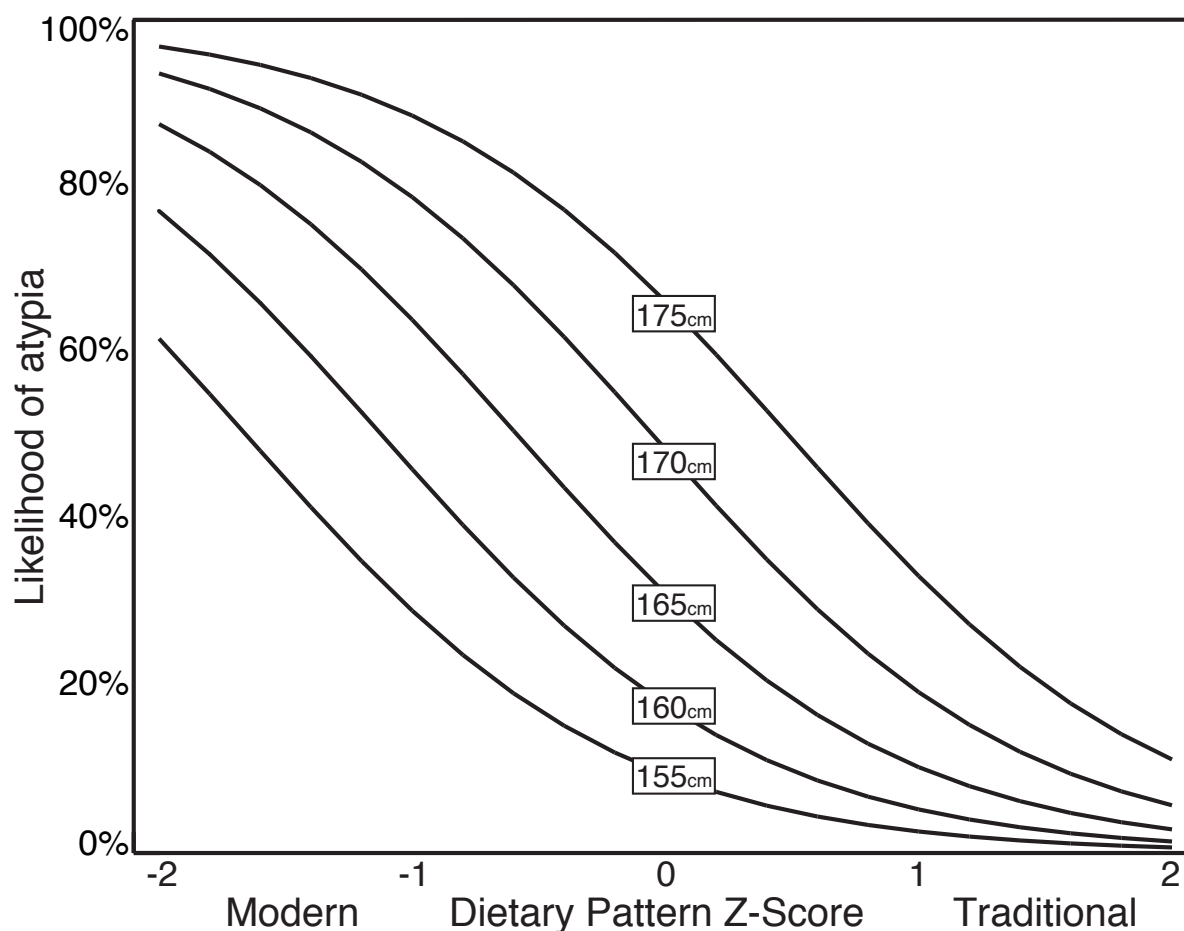


Figure 11: **A Model of having a Breast Cancer Risk Biomarker based on the Height and Diet of High-Risk, Middle-Class American Women Younger than 50yrs.** Lower height and greater adherence to a Traditional dietary pattern predicted a lower likelihood of having atypia. The AUC statistic for the model was 0.83.

The Modern-Traditional dietary pattern defined herein differs from the Mediterranean diet in one major way: the respective negative versus positive loading of grains. Similar multivariate dietary patterns, i.e. higher intake of fish, chicken, and vegetables, are associated with lower breast cancer risk in Greece (86), Spain (45), France (96), Uruguay (103), Korea (95), and China (109). Although other studies have identified nearly identical dietary patterns that were not significantly associated with breast cancer risk (58, 93), our findings support the common epidemiologic observation that eating more vegetables, fish, and poultry is associated with lower breast cancer risk.

The Modern-Traditional diet also incorporated components of a Western diet (210), e.g., negatively loading with grains, glycemic load, added sugar, and trans fat. Diets associated with a higher breast cancer risk are characterized by a high consumption of sweet baked goods, ice cream, processed meat (92), vegetable oil, candy, refined versus whole grains (108), and refined grains and meat (109). Again, however, not all studies have found a Western dietary pattern that is significantly associated with breast cancer risk (58, 93).

Overall, a dietary pattern with a higher micronutrient plus antioxidant to energy ratio appears protective (37). Diets filled with more energy and less micronutrients may fuel carcinogenesis. For example, consuming calorically-dense foods like baked goods and sweets is associated with a greater risk of breast cancer (44). Among sources of carbohydrates, fruits and vegetables appear protective against breast cancer (25). The Modern-Traditional dietary pattern was positively loaded with several carotenoids. Fruits and vegetables are rich sources of carotenoids and women with higher levels of carotenoids in plasma are less likely to develop breast cancer (214). Importantly, the DHQ-I includes juices, jellies, and pies in estimates of fruit intake, which may explain why fruit was not a component of a protective dietary pattern.

Our study has limitations. The small sample size is partially offset by our extensive phenotyping, which included fatty acid analysis of five lipid compartments. Complex models of atypia were not constructed to avoid overfitting our sample. It will be important to validate this dietary pattern as a significant predictor of breast cancer risk in another population. Another limitation is the absence of measuring physical activity, which is negatively associated with both breast cancer risk (215) and adherence to a Western dietary pattern (104). Therefore, this cross-sectional study cannot make claims about the dietary influence on atypia prevalence; our results only indicate that, among mostly Caucasian, middle- to upper-class, Midwestern women at an elevated risk of breast cancer, those that tend to eat more grains, dairy, trans fat, and added sugar



rather than vegetables, fish, alcohol, and poultry exhibit a tissue biomarker associated with a higher likelihood of developing breast cancer. Lastly, self-reported dietary behavior measured by a food frequency questionnaire, within the context of a high-risk breast cancer prevention clinic, is susceptible to several biases (136, 216).

In conclusion, we identified and tissue-validated a Modern-Traditional dietary pattern that was inversely associated with a biomarker of short-term risk of developing breast cancer. Women interested in lowering their risk of developing breast cancer may benefit from avoiding carbohydrate-rich processed foods cooked with partially-hydrogenated vegetable oils. Our findings justify exploration of cytologic atypia as a surrogate endpoint in a dietary intervention of replacing grains, added sugar, and sources of trans fat with vegetables, fish, and poultry to reduce breast cancer risk.

## **Chapter Six:**

## **Conclusion**

### *Summary of Findings*

We observed several important dietary trends in this sample of premenopausal and postmenopausal women with a higher-than-average risk of developing breast cancer. First, this sample consumed about ten times more n-6 PUFA than n-3 PUFA; the median (IQR) of total n-3:n-6 in plasma TAGs was 1:11 (8 to 14). Second, this is concerning, because an imbalanced n-3:n-6 PUFA ratio was predictive of atypia status. We found a protective association between n-3 PUFA and breast cancer risk. Women with higher levels of long-chain n-3 PUFA in circulation were less likely to exhibit atypia in RPFNA. Third, the density of nutrients was more predictive of atypia status for premenopausal compared to postmenopausal participants. In particular, we found the protective associations for higher n-3 PUFA and soy intake were very strong for younger, premenopausal patients and absent among those postmenopausal. We identified a Modern-Traditional dietary pattern defined by fish, poultry, and vegetable consumption versus grains, dairy, trans fat, and sugar. The blood and breast tissue content of n-3 PUFA, n-6 PUFA, and *trans* fatty acids substantiated this dietary pattern. The Modern-Traditional dietary pattern predicted atypia status among younger women. Taken together, a diet loaded with empty calories largely consisting of grains infused sugar, n-6 PUFA, and *trans* fats may accelerate breast cancer development, while a diet that has a higher density of nutrients (n-3 PUFA, carotenoids, and B-vitamins) from fish, poultry, and vegetables may protect against breast tumor formation, especially for younger women.

### *Limitations*

This research represents a modest contribution toward understanding how diet influences breast cancer risk. The use of a biomarker as a proxy for breast cancer risk in a small, homogenous sample limits broad, sweeping conclusions. Atypia does not predict who will or will not develop breast cancer, it only conveys relative likelihood. As opposed to case-control

studies, a prognostic marker precludes someone's diagnosis affecting his or her (a) recollection of behavior or (b) biomarkers, i.e., reverse causality. However, the dietary information collected from women at a high-risk clinic may be skewed by patients' (conscious and unconscious) desire to be viewed favorably by staff. Honesty may partially explain why higher alcohol intake was incorporated into a protective dietary pattern, given that alcohol is known to contribute to breast cancer risk. And lastly, as discussed before, the sample size and performance of multiple statistical tests requires that others replicate these observations.

### *Future Directions*

Usually in science, research leads to more questions (and testable hypotheses) than answers. After finding low n-3 PUFA in tissue of women with atypia, the BCPC explored the effects of 6 month, high-dose supplementation of long-chain n-3 PUFA on RPFNA cytology in premenopausal and postmenopausal women [in review]. If supplementation corrects cytologic abnormalities by restoring n-3:n-6 PUFA balance, then one would hypothesize that women with the lowest levels of long-chain n-3 PUFA and n-3:n-6 PUFA ratios would be most likely to exhibit a favorable response (no longer evidencing atypia after taking the supplements). The capacity of fatty acid levels and other biomarkers, e.g., systemic and local inflammation, to predict cytologic response to supplementation could be explored using the results from the aforementioned trials. Classification tree analysis would be an ideal statistical tool for such an endeavor, because the data-driven technique identifies the most valuable measurement(s) among large sets of variables (217).

The nutrient-centered analysis identified soy, niacin, and n-3 PUFA as independently predictive of atypia status among premenopausal participants. The protective effects of soy and n-3 PUFA on mammary tumor development in preclinical models are well-established (194, 196). Niacin can protect against leukemia in rats (218), but niacin deprivation/dietary-enrichment

has not been tested on mammary tumor development. The interactive effects of soy, niacin, and n-3 PUFA on mammary tumorigenesis could be explored in a preclinical study; rodents predisposed to develop mammary tumors, by mutagen administration or genetic manipulation, would be placed on a lifelong diet of a) control, b) n-3 PUFA, c) soy, d) niacin, e) n-3 PUFA+soy, f) n-3 PUFA+niacin, g) soy+niacin, or h) n-3 PUFA+soy+niacin. Using tumor incidence, multiplicity, and weight as endpoints, such a study would establish antagonistic and/or synergistic effects of these nutrients on mammary tumorigenesis.

*Trans* fats were implicated as risk-associated in both nutrient and dietary pattern analyses. One logical next step would be to test the feasibility of a dietary intervention aimed at reducing *trans* fat consumption. Levels of *trans* fatty acids in circulating lipid compartments would be appropriate endpoints in a feasibility study. Importantly, products can still contain *trans* fats even though their nutrition label lists “0 grams” if the serving size contains less than 1 gram; therefore, independent analysis of fatty acid content of food products may be necessary to identify dietary sources. Researchers could also incorporate reduction of *trans* fat intake into a dietary intervention for breast cancer prevention.

The Modern-Traditional dietary pattern needs to be tested for its capacity to predict breast cancer risk in another sample. The pattern’s name should be confirmed by a repeated cohort effect, i.e., correlation with age. If the dietary pattern reflects general health-conscious behavior, then women with a more Traditional diet would also have a lower prevalence of tobacco smoking and report more leisure physical activity. Recalculating the score without each component and reassessing the association with breast cancer would illuminate the importance of the dietary pattern’s individual components. It was surprising to observe alcohol intake positively contributing to a dietary pattern that was inversely associated with breast cancer risk status; this needs to be elucidated. If the Modern-Traditional dietary pattern reproducibly

correlates with breast cancer risk, then it should be formally tested with a randomized controlled trial. Looking more broadly, the dietary pattern may also help explain risk of other lifestyle-related chronic diseases.

It would be helpful for future research to gather more information about participants' genotype and nutritional status to better understand the relationship between PUFA and breast cancer risk. For example, genetic variation of the desaturases (enzymes involved in PUFA metabolism) can strongly influence levels of long-chain n-3 and n-6 PUFA; one report found that genetic differences explained 25% of the variance in arachidonic acid (AA) levels (219). Others have hypothesized that genetic variation of cyclooxygenase-2, which converts EPA, DHA, and AA into inflammation-regulating messengers, could influence breast cancer risk (220). If interactions are present, then genotyping will be essential.

Lipid-soluble antioxidants (tocopherols and tocotrienols) have been reported to interact with PUFA when affecting mammary tumor processes in both preclinical (221) and epidemiologic research (222, 223). Similarly, selenium status would be a valuable measurement, because selenium is an essential component of glutathione peroxidase, an antioxidant enzyme (224). Multiple vitamins and minerals are known to interface with PUFA. As examples, zinc and iron deficiencies impair PUFA metabolism in rodents (225, 226). Inducing a marginal vitamin B6 deficiency in healthy humans lowers plasma levels of EPA, DHA, and AA (227). Although cost impedes gathering additional measurements, extensive nutritional profiling is the clearest way to untangle the network of nutrients. Interventions designed with an understanding nutrient networks may lead to breakthroughs for preventing diseases as complex as breast cancer.

A Food Frequency Questionnaire (FFQ) generated the dietary information collected in this research. Unfortunately, FFQs are notoriously inaccurate compared to food records and 24-hour recalls (228). Technology may eventually enhance accuracy of food and drink consumption

measurements. As of now, photographic food records have demonstrated equal precision compared to food records, with favorable feedback (easier to use) from parents with young children (229), adolescents (230), and (even older) adults (231). We used tissue fatty acids to enhance the veracity of dietary data; fecal bacteria represent an analogous measurement because they also convey information about dietary behavior (232) and are associated with human health (233). Poor dietary assessment from FFQs has been blamed as the source of inconsistent and null results from studies of nutrition and cancer (228). Hopefully, future research will more accurately measure what humans eat and drink so that we can better understand how diet quality influences disease risk.

Meal frequency and timing is an important aspect of dietary behavior that was not measured in this study. Emerging evidence indicates that intermittent dietary restriction can counteract the negative metabolic effects of a high-fat (mostly n-6 PUFA) diet (234). The periods of no food intake appear to induce stress responses that activate repair pathways (235), which are important for mediating the cancer-preventive effects of calorie restriction (236). As a proxy for meal timing, working at night is associated with higher breast cancer risk (237, 238). There are currently no publications analyzing meal frequency and breast cancer risk.

Future trials testing the effects of changing diet to reduce breast cancer risk may need to be designed differently than they have been. Typically, a comparison group is given standard nutrition advice, i.e., follow the country's nutritional guidelines, and the intervention group receives nutrition counseling, i.e., reduce the portion of energy intake from fat sources by increasing vegetable and whole grain consumption (7). Nutrition counseling could be improved by food-based guidance with simple rules (40, 239) to enhance compliance. Nutrient-centered advice can require math (240) and the ability to navigate a nutrition label (241). Interventions may also be more effective if they better addressed the major barriers to healthy eating: lack of

time, giving up favorite foods, willpower, and cost (242). Food vouchers (to reduce cost), cooking classes (to replace favorite foods and teach quick preparation of healthful meals), and family-based interventions (to increase social support for behavior change) are potential solutions. In dietary intervention trials, supplementing participants with food/meals has demonstrated favorable results (84, 243), as has a family-centered approach (244). In nutrition research, the major tradeoffs in dietary intervention are between cost per participant and average behavior change from the dietary intervention, i.e., getting participants to eat and drink as recommended. These issues should be given careful consideration when designing clinical trials aimed at changing dietary behavior, especially for the prevention of breast cancer, because effects may be long delayed and thus require lengthy (expensive) follow-up.

#### *Closing Statement*

All biological processes are a consequence of genes interacting with environment. Genes are set, but we can change our environment. My research has attempted to understand how one part of the environment (diet) influences breast cancer risk in order to empower women with accurate information. In this sample of women, those with the highest short-term risk could be identified by the types of fat found in their tissue, the nutrient density of their diet, and their overall dietary pattern. Although much more time, energy, and resources are needed to make evidence-based, dietary recommendations to reduce breast cancer risk, this research reiterates the fact that choices matter.



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Supplemental Table 1: Methods of Dietary Patterns and Breast Cancer Risk Publications

#	Year	Country	Population	Methods
1	2001	Sweden	61,463 women, 9.6 years follow-up;	Cohort; FFQ; Varimax rotation; 3 patterns; Quintiles
2	2004	Italy	9000 women, age 34-70 years	Cohort; FFQ; Varimax rotation; 4 patterns; Tertiles
3	2005	United States	Nurses; aged 30-55; Postmenopausal breast cancer; 71,000 women Followed for up to 16 years	Cohort; FFQ; Factor analysis (unknown rotation); 2 patterns; Quintiles
4	2005	United States	Nurses; aged 25 to 42; 90,638 Premenopausal women; 8 years of follow-up	Cohort; FFQ; Varimax rotation; 2 patterns; Quintiles;
5	2005	United States	40,559 women; Postmenopausal;	Cohort; FFQ Varimax rotation; 3 patterns; Quintiles
6	2008	Germany	15,351 women; Age 35-65	Cohort; FFQ; reduced rank regression; 1 pattern; tertiles
7	2008	Italy	2569 cases, 3413 controls; hospital-based controls; >60% postmenopausal	Case-control; FFQ; Varimax rotation; 4 patterns; Tertiles
8	2008	United States	2281 cases, 2468 controls; community based controls; 1624 Hispanic, 3122 non-Hispanic white; 65% postmenopausal	Case-control; FFQ; Varimax rotation; 5 patterns; Quartiles
9	2009	United States	Asian American; 1248 cases, 1148 controls;	Case-control; FFQ; Mediterranean; Factor analysis (unknown rotation); 4 patterns; Quartiles
10	2009	France	Postmenopausal; 65,000 women	Cohort; FFQ; Varimax rotation; 2 patterns; Quartiles
11	2009	Uruguay	461 cases, 2532 hospital-based controls; Premenopausal and Postmenopausal	Case-Control; FFQ; Varimax rotation; 4 patterns; Tertiles
12	2009	United States	African American; 50,000 women; Age 21-69; 77% Premenopausal	Cohort; FFQ; Varimax rotation; 2 Patterns; Quintiles
13	2010	Korea	357 cases, 357 controls; Age 25-77; 40% postmenopausal	Case-control; FFQ; Factor analysis (unknown rotation); 2 patterns; Tertiles
14	2010	Uruguay	442 cases, 442 hospitalized controls	Case-control; FFQ; Promax rotation; 2 patterns; quartiles
15	2010	China	34,000 women; Postmenopausal	Cohort; FFQ; Mediterranean diet; factor analysis (unknown rotation); 3 patterns; quartiles
16	2010	Uruguay	111 cases, 222 controls; Premenopausal and postmenopausal	Case-control; FFQ; Varimax rotation; 6 patterns; tertiles
17	2011	Australia	21,000 women; Premenopausal and Postmenopausal; Age 27-76	Cohort; FFQ; Varimax rotation; 4 patterns; Quintiles
18	2011	Mexico	1000 cases, 1074 controls; Age 35 to 69;	Case-control; FFQ; Varimax rotation; 1 pattern; tertiles
19	2011	China	438 cases, 438 controls; 25-70 yrs;	Case-control; FFQ; Varimax rotation; 2 patterns; Quartiles

Supplemental Table 1: Methods of Dietary Patterns and Breast Cancer Risk Publications (*continued*)

#	Year	Country	Population	Methods
20	2011	Germany	Postmenopausal; 2884 cases, 5509 controls; 50-79 yrs;	Case-control; FFQ; Varimax rotation; 2 patterns; Quintiles
21	2012	Cyprus	935 cases, 817 controls; age 40-70; Postmenopausal	Case-control; FFQ; Mediterranean diet (x2); Oblimin rotation; 5 patterns; Quartiles
22	2012	France	437 cases, 922 controls; Age 25-85	Case-control; FFQ; Varimax rotation; 3 patterns; standard error increment
23	2013	Sweden	Initial age 30 to 49; 49,000 women	Cohort; FFQ; Mediterranean diet; 1 pattern; Quintiles
24	2013	Tanzania	115 cases, 230 controls	Case-control; FFQ; varimax rotation; 4 patterns; unknown quantiles or standard error increment
25	2013	Malaysia	382 cases, 382 controls	Case-control; FFQ; HEI-2005; 1 pattern; Quartiles
26	2013	Argentina	100 cases; 294 controls; Non-hospital controls;	Case-control; FFQ; Varimax rotation; 4 patterns; Tertiles;
27	2013	United States	91,779 women; 43% Premenopausal	Cohort; FFQ; Varimax rotation; 5 patterns; Quintiles
28	2014	United Kingdom	610 cases, 1891 controls; 19% Premenopausal;	Nested case-control; Food diaries; Mediterranean, Varimax rotation; Reduced rank regression; 4 patterns; Tertiles;
29	2014	Spain	1017 cases, 1017 controls; Premenopausal and Postmenopausal	Case-control; FFQ; principal components analysis (no rotation); Mediterranean; Alternate Healthy Index; 5 patterns; Quartiles

Studies are listed in chronological order. The following table organizes the results of these studies into general categories of dietary patterns and statistically significant associations.

Supplemental Table 2: Results of Dietary Patterns and Breast Cancer Risk Publications

Category <sup>a</sup>	Risk	# <sup>b</sup>	Name <sup>c</sup>	Loadings <sup>d</sup>	Results <sup>e</sup>
Drinker/ Alcohol	High	1	Drinker	Whole grains, Poultry, Wine, Liquor, Beer, Snacks	High-risk; p=0.002; p=0.002 for >50 years old
		5	Traditional Southern (inverse)	Cooked greens, Beans and legumes, Sweet potatoes, Cornbread, muffins, and tortillas, Coleslaw, cabbage, and sauerkraut, Fried fish, [Cheese and cheese spread, Mayonnaise and salad dressing, Wine, Liquor]	Protective; p=0.001; only among those without family history; more predictive among normal BMI; more protective among smokers p=0.008; most protective against ER+/PR+ tumors; Significant individual foods were a) Beans and legumes and b) Mayonnaise and salad dressing
		10	Alcohol/Western	Potatoes, Rice, Pasta, Semolina, French fries, Appetizers, Pizza, Sandwiches, Cakes, Processed Meat, Ham, Eggs, Canned Fish, Crustaceans, Mayonnaise, Butter/cream, High-alcohol beverages	High-risk; p=0.007; p=0.005 for ER+/PR+ tumors; p=0.001 for normal BMI
		11	Drinker	Beer, Wine, Hard Liquor	High-risk; p=0.02
		22	Meat-eaters and drinkers	Mollusc and shellfish, Meat, Processed meats, Offal and giblets, Wine, Alcohol (not wine)	High-risk; p<0.05
		27	Salad and wine	Green salad, Fish, Wine and champagne, Salad dressing or mayonnaise (low-fat), Coffee and tea, Tomatoes and tomato juice	High-risk; p=0.01; most risky for ER+/PR+ tumors p<0.001
		28	High alcohol	Wine, Beer, Cider	High-risk; p=0.04
		2	Prudent	Leafy vegetables, Other fruiting vegetables, Carrots, Pulses, Rice, Poultry, Fish, [Wine, Sprits]	All p>0.05
	Low	8	Mediterranean	Liquor, Poultry, Seafood, Vegetables, Salad greens, High-fat salad dressings	Protective; p<0.01 overall; p<0.01 for postmenopausal Hispanic; p=0.03 for obese pre/peri-menopausal; p=0.04 for overweight postmenopausal

<sup>a</sup> General categories of dietary patterns. <sup>b</sup> Relates Supplemental Table 2 back to Supplemental Table 2. <sup>c</sup> Names bestowed by the authors. <sup>d</sup> Loadings include the foods and nutrients contributing to the dietary pattern with a factor loading coefficient of  $\geq 0.30$  (absolute value) with brackets [ ] indicating a negative contribution. <sup>e</sup> Summary of statistically significant results.

Supplemental Table 2: Results of Dietary Patterns and Breast Cancer Risk Publications (*continued*)

Category <sup>a</sup>	Risk	# <sup>b</sup>	Name <sup>c</sup>	Loadings <sup>d</sup>	Results <sup>e</sup>
Western/ Unhealthy	High	3	Western	Refined grains, Desserts and sweets, Processed meats, Red meats, French fries, Condiments, Potatoes, Pizza, Full-fat dairy products, Sweetened beverages, Mayonnaise, Margarine	Unclear overall; High-risk among smokers p=0.03
		10	Alcohol/ Western	Potatoes, Rice, Pasta, Semolina, French fries, Appetizers, Pizza, Sandwiches, Cakes, Processed Meat, Ham, Eggs, Canned Fish, Crustaceans, Mayonnaise, Butter/cream, High-alcohol beverages	High-risk; p=0.007; p=0.005 for ER+/PR+ tumors; p=0.001 for normal BMI
		11	Western	Fried meat, Barbequed meat, Processed meat, Eggs, Desserts, Cooked vegetables	High-risk; p<0.0001
		16	Western	Beef, Lamb, Hamburger, Processed meat, Butter, Fried eggs, All desserts, French fries	High-risk; p=0.03
		16	Fried white meat	Milanesa, Hamburger, Poultry skin, Fried fish, Baked fish, Common oil, Potatoes, [Olive oil, Raw vegetables]	Risk associated; p=0.009
		19	Refined grain-Meat-Pickle	Refined grains, Processed meat, Pork, Beef, Lamb, Organ meat	High-risk; p<0.001
		26	Traditional	Fat meat, Bakery products, Vegetable oils and mayonnaise	High-risk; p<0.01
		26	Rural	Pulses, Starchy vegetables, Processed meat, Bakery products, Candies, Added sugar and sweets	High-risk; p<0.01
		29	Western	High-fat dairy, Processed meat, Refined grains, Sweets, Caloric drinks, Convenience food and sauces, [Low-fat dairy, Whole grains]	High-risk; p=0.02; p=0.01 for premenopausal
		8	Western	High-fat dairy, Refined grains, Gravy and sauces, Fast foods, Red and processed meats, Potatoes, Margarine, Polyunsaturated fat, High-fat and high-sugar desserts	Risk-associated; p<0.01 overall; p<0.01 for non-Hispanic white; p<0.01 for normal BMI postmenopausal

<sup>a</sup> General categories of dietary patterns. <sup>b</sup> Relates Supplemental Table 2 back to Supplemental Table 2. <sup>c</sup> Names bestowed by the authors. <sup>d</sup> Loadings include the foods and nutrients contributing to the dietary pattern with a factor loading coefficient of  $\geq 0.30$  (absolute value) with brackets [ ] indicating a negative contribution. <sup>e</sup> Summary of statistically significant results.

Supplemental Table 2: Results of Dietary Patterns and Breast Cancer Risk Publications (*continued*)

Category <sup>a</sup>	Risk	# <sup>b</sup>	Name <sup>c</sup>	Loadings <sup>d</sup>	Results <sup>e</sup>
Western/ Unhealthy ( <i>continued</i> )	Null	1	Western	Processed meat, Sweets, Refined grains, High-fat dairy, Meat, Soda, Potato, Pea soup	All p>0.05
		2	Western	Potatoes, Other pasta, Beef, Veal, Pork, Processed meat, Offal, Eggs, Seed oils, Butter, Cakes	All p>0.05
		4	Western	Refined grains, Desserts, Red meat, Processed meats, French fries, Pizza, Potatoes, Snacks, Eggs, High-sugar drinks, Margarine, High-fat dairy products, Mayonnaise, Nuts	All p>0.05
		5	Beef/pork-starch	Pork, Beef, Bacon, Hamburger, French fries and fried potatoes, Sausage, Fried chicken, [Bran and granola cereal, Skim milk, Broiled/baked chicken, Fish (not fried)]	All p>0.05
		9	Western meat/starch	Pasta with meat, Beef taco, Beef burrito, Pizza, Meatballs, Hamburger, Fried potatoes, Baked potatoes, Mashed potatoes, Pancake, Bagels	All p>0.05
		12	Western	Refined grains, High-fat dairy products, Meat, Processed meat, Eggs, Oils, French fries, Potato, Sweets, Soda, Snacks	All p>0.05
		18	Western	Mayonnaise, Oils, Vegetable oils, Animal fats, Typical Mexican dishes, Processed foods, Refined cereals, Chili, Fatty dairy products, Sweetened beverages, Corn, Red meats, Eggs	All p>0.05
		22	Western	Cereals, Cheese, Eggs, Processed meats, Butter, Oil (not olive), Sweets, Pizza	All p>0.05
		27	High-protein, high-fat	Butter, margarine, or fat added to vegetables, Beef roasts, steaks, and sandwiches, Sausage and bacon, Pork, Hamburgers and cheeseburgers, Fried chicken, Beef stew or pot pie with vegetables, Eggs, Fried potatoes, Butter on bread or rolls, Salad dressing or mayonnaise (regular fat)	All p>0.05

<sup>a</sup> General categories of dietary patterns. <sup>b</sup> Relates Supplemental Table 2 back to Supplemental Table 2. <sup>c</sup> Names bestowed by the authors. <sup>d</sup> Loadings include the foods and nutrients contributing to the dietary pattern with a factor loading coefficient of  $\geq 0.30$  (absolute value) with brackets [ ] indicating a negative contribution. <sup>e</sup> Summary of statistically significant results.

Supplemental Table 2: Results of Dietary Patterns and Breast Cancer Risk Publications (*continued*)

Category <sup>a</sup>	Risk	# <sup>b</sup>	Name <sup>c</sup>	Loadings <sup>d</sup>	Results <sup>e</sup>
Western/ Unhealthy ( <i>continued</i> )	Low	13	Meat-Starch	Other seafood, Fatty fish, Cakes, Pizza, Processed meats, Red meat, Bread, Poultry, Noodles, High-fat red meat, Red meat byproducts, Dairy products, Oil, Snacks, Carbonated beverages, Seafood products, Sweets, Eggs	Overall p>0.05; Protective among postmenopausal p=0.009
		20	Unhealthy	Processed meat, Red meat, Garlic/onions, Deep-frying fat	Overall p>0.05; Protective against ER-/PR- tumors p=0.02
	High	8	Prudent	Low-fat dairy, Whole grains, Fruits and fruit juices, Legumes, Vegetables, Soups	Risk-associated; p<0.01 overall; p<0.01 for postmenopausal non-Hispanic white;
Healthy/ Prudent/ Vegetables/ Fruits	Null	1	Healthy	Vegetables, Fruit, Fish, Whole grains, Low-fat dairy, Poultry, Cereal, Eggs, Meat	All p>0.05
		2	Prudent	Leafy vegetables, Other fruiting vegetables, Carrots, Pulses, Rice, Poultry, Fish, [Wine, Sprits]	All p>0.05
		4	Prudent	Other vegetables, Leafy vegetables, Fruit, Dark yellow vegetables, Cruciferous vegetables, Legumes, Tomatoes, Fish, Poultry, Onions, Whole grains, Salad dressing, Fruit Juice, Low-fat dairy Green salad, Broccoli, Fish, Chicken, Carrots, Tomatoes and tomato juice, Spinach, Apples, applesauce, and pears, [Doughnuts, cookies, and cakes]	All p>0.05
		5	Vegetable-fish/poultry-fruit	Poultry skin, Total grains, Raw vegetables, Cooked vegetables, Legumes, Citrus fruits, Other fruits Capsicum (bell peppers), Salad greens, Cucumber, Celery/fennel, Beet, Coleslaw, Potato without fat, Carrot, Cabbage/brussel sprouts, Cauliflower, Broccoli, Leafy greens, Green beans/peas, Pumpkin, Zucchini/squash/eggplant	All p>0.05
		16	Prudent	Fruits, Fruiting/leafy/other vegetables, Garlic/onions, Oil and vinegar dressing, Mayonnaise	All p>0.05
		17	Vegetable	Fruits, Dried fruits, Raw vegetables, Cooked vegetables, Olive oil	All p>0.05
		20	Healthy		
		22	Mediterranean		

Supplemental Table 2: Results of Dietary Patterns and Breast Cancer Risk Publications (*continued*)

Category <sup>a</sup>	Risk	# <sup>b</sup>	Name <sup>c</sup>	Loadings <sup>d</sup>	Results <sup>e</sup>
Healthy/ Prudent/ Vegetables/ Fruits ( <i>continued</i> )	Null ( <i>cont.</i> )	29	Prudent	Low-fat dairy, Leafy vegetables, Fruiting vegetables, Root vegetables, Other vegetables, Fruits, Juices	All p>0.05
		2	Salad vegetables	Mixed vegetables in salad, Leafy vegetables, Raw tomatoes, Other fruiting vegetables, Carrots, Olive oil	Protective; p=0.02; p=0.001 among normal BMI
		3	Prudent	Other vegetables, Leafy vegetables, Cruciferous vegetables, Fruit, Yellow vegetables, Legumes, Fish, Tomatoes, Poultry, Whole-grain products, Low-fat dairy products, Salad dressings, Garlic	Overall p=0.43; p=0.006 for ER- tumors; fruits and vegetables independently associated with lower ER-risk.
		9	Vegetables/soy	Green beans/peas, Carrots, Cabbage, Bean sprouts, Green peppers, Bok choy, Fresh tofu, Fresh soybeans, Soy milk	Protective; p=0.008
		10	Healthy/Mediterranean	Fruits, Raw vegetables, Cooked vegetables, Crustaceans, Fish, Olive oil	Protective; p=0.003; p=0.001 for ER+/PR- tumors; more protective among those with low energy intake
	Low	11	Prudent	Poultry, Fish, Raw vegetables, Cooked vegetables, Fruits	Protective; p=0.005
		12	Prudent	Cruciferous vegetables, Other vegetables, Tomatoes, Fruit, Whole grains, Fish, Low-fat dairy products, Poultry, Juice, Soup, Beans, Pasta	Overall p=0.06; p=0.01 for normal BMI; p=0.01 for premenopausal;
		13	Vegetable-Seafood	Green/yellow vegetables, Condiments, Light colored vegetables, Shellfish, Mushrooms, Tubers, Seaweeds, Tofu/soy milk, Bonefish, Other seafood, Lean fish, Fatty fish, Fruits, Kim chi, Salted fermented seafood, Fruit products, Red meat	Protective; p<0.0001; (stratified) p<0.0001 for premenopausal, postmenopausal, ER+/PR+ tumors, and ER-/PR- tumors
		14	Vegetable-Fruit-Soy	Cauliflower, Broccoli, Carrots, Green beans/peas, Tofu, Gum jum, Tou gay, Tung goo, Tomatoes, Yin choy, Corn, Lettuce, Orther Tau kwa, White potatoes, Kai lan, Pak choy, Choi sum, Head cabbage, Fu kua, Watercress	Protective; p=0.03; p=0.01 postmenopausal

<sup>a</sup> General categories of dietary patterns. <sup>b</sup> Relates Supplemental Table 2 back to Supplemental Table 2. <sup>c</sup> Names bestowed by the authors. <sup>d</sup> Loadings include the foods and nutrients contributing to the dietary pattern with a factor loading coefficient of  $\geq 0.30$  (absolute value) with brackets [ ] indicating a negative contribution. <sup>e</sup> Summary of statistically significant results.

Supplemental Table 2: Results of Dietary Patterns and Breast Cancer Risk Publications (*continued*)

Category <sup>a</sup>	Risk	# <sup>b</sup>	Name <sup>c</sup>	Loadings <sup>d</sup>	Results <sup>e</sup>
Healthy/ Prudent/ Vegetables/ Fruits ( <i>continued</i> )	Low ( <i>cont.</i> )	17	Fruit	Orange/mandarin, Apple, Peach/nectarine, Pear, Canteloupe/honeydew, Watermelon, Strawberry, Plum, Apricot, Fig, Grape	Protective; p=0.03; p=0.004 for ER- tumors; p=0.01 for PR- tumors
		19	Vegetable-Fruit-Soy-Milk-Poultry-Fish	Total dairy products, Fruit, Egg, Fruit juice, Vegetable, Poultry, Soy	Protective; p<0.001
		21	Fruit/ Vegetables/ Fish/ Legumes	Fish, Vegetables/salad, Fruit, Legumes	Protective; p<0.0001
		26	Prudent	Pulses, Lean meat, Non-starchy vegetables, Fruits	Protective; p<0.01
		27	Plant-based	Peaches and apricots, Strawberries and other berries, Carrots and mixed vegetables with carrots, Apples and apple sauce, Other fruit, Oranges, Broccoli, Bananas, Watermelon, Cantaloupe, Other vegetables, String beans and green beans, Peas, Cauliflower and brussel sprouts	Protective; p=0.003; p=0.03 for ER-/PR- tumors
		29	Mediterranean	White fish, Oily fish, Seafood/shellfish, Leafy vegetables, Fruiting vegetables, Root vegetables, Other vegetables, Legumes, Potatoes, Fruits, Olive and other vegetable oils, [Juices]	Protective; p<0.01; most protective against triple-negative tumors p<0.01
		8	Mediterranean	Liquor, Poultry, Seafood, Vegetables, Salad greens, High-fat salad dressings	Protective; p<0.01 overall; p<0.01 for postmenopausal Hispanic; p=0.03 for obese pre/peri-menopausal; p=0.04 for overweight postmenopausal

<sup>a</sup> General categories of dietary patterns. <sup>b</sup> Relates Supplemental Table 2 back to Supplemental Table 2. <sup>c</sup> Names bestowed by the authors. <sup>d</sup> Loadings include the foods and nutrients contributing to the dietary pattern with a factor loading coefficient of  $\geq 0.30$  (absolute value) with brackets [ ] indicating a negative contribution. <sup>e</sup> Summary of statistically significant results.



Supplemental Table 2: Results of Dietary Patterns and Breast Cancer Risk Publications (*continued*)

Category <sup>a</sup>	Risk	# <sup>b</sup>	Name <sup>c</sup>	Loadings <sup>d</sup>	Results <sup>e</sup>
Ethnic/ Traditional	High	9	Ethnic meat/starch	Pork/fish soups, liver, pork spareribs, Salted/dried fish, Fried shellfish, Chicken wings, Rice, Fried/Spanish rice, Fried noodles, Fried dim sum	High-risk; p=0.008
	Null	15	Meat-dim sum	Siew mai, Other steamed snack, Otter otter, Gravy noodle, Chicken rice, Steamed meat bao, Popiah, Puffs, Chinese rojak, Pork satay, Ngor hiang, Deep fried chicken, Chicken satay, Coconut desserts, Glutinous rice dumpling, Coconut rice dishes, Chicken mutton curry, Preserved eggs, Sweet kuey, Roasted duck or goose	All p>0.05
		24	Mchicha diet	Bread, Mchicha, Cucumber/okra, Onion, Carrots and tomatoes, Maize, Fish, Avocado	All p>0.05
		27	Ethnic	Lentil, pea, and bean soups, Beans, Tofu, Vegetable soups, Rice, Meat substitutes from soy, Mustard, turnip greens, and collards, Sweet potatoes	All p>0.05
	Low	5	Traditional Southern	Cooked greens, Beans and legumes, Sweet potatoes, Cornbread, muffins, and tortillas, Coleslaw, cabbage, and sauerkraut, Fried fish, [Cheese and cheese spread, Mayonnaise and salad dressing, Wine, Liquor]	Protective; p=0.001; only protective if negative family history; more predictive among normal BMI; more protective among smokers; most protective against ER+/PR+ tumors; Significant individual foods were a) Beans and legumes and b) Mayonnaise and salad dressing
		11	Traditional	Eggs, Dairy, Desserts, Total Grains, Tubers, Fruits	Protective; p=0.002
		17	Traditional Australian	Sweet biscuits, Cakes/sweet pastries, Puddings, Margarine, Sausage, Potato without fat, Tea, [Olive oil, Salad greens, Cucumber]	Overall p=0.24; p=0.04 for those <56yrs old at follow-up
		8	Native Mexican	Mexican cheeses, Mexican soups, Mexican meat dishes, Legumes, Tomato-based sauces	Protective; p<0.01 overall; p≤0.05 for non-hispanic white and pre/peri-menopausal Hispanic; p<0.01 for normal BMI pre/peri-menopausal; p=0.02 for normal BMI postmenopausal;

Supplemental Table 2: Results of Dietary Patterns and Breast Cancer Risk Publications (*continued*)

Category <sup>a</sup>	Risk	# <sup>b</sup>	Name <sup>c</sup>	Loadings <sup>d</sup>	Results <sup>e</sup>
High Carbohydrate	High	26	Starchy	Refined grains, Added sugar and sweets, [Whole grains]	High-risk; p<0.01
		7	Starch-rich	Vegetable protein, Starch, Sodium, Phosphorus, Iron, Zinc, Thiamin, Vitamin B6, Niacin, Lycopene	Risk-associated; p<0.01
	Null	21	Cakes/Sweets/Nuts/Crackers/Pasta/Rice	Cakes, Chocolate, Bakery, Nuts, Crackers/biscuits, Pasta/rice	All p>0.05
		28	High fiber	Fresh fruit, Raw/boiled vegetables, High-fiber bread, High-fiber breakfast cereals	All p>0.05
	Low	27	High-carbohydrate	Fried potatoes, Burritos and tacos with meat or beans, Pizza, Salsa and ketchup, Tortillas, Spaghetti and other pasta, Bagels, buns, and English muffins	Overall p=0.11; p=0.05 for ER+/PR- tumors
High Fat	High	6	High-fat	Processed meat, Fish, Butter, Margarine, [bread, fruit juices]	High-risk; p=0.001
		16	Low fat (inverse)	Skinless poultry, Butter, Skim milk, Low-fat yogurt, coffee, [Poultry skin, Whole milk]	Protective; p=0.001
		24	Fatty diet	Red meat, Milk, Butter/lard, Mixed vegetable fats and oil, [Sunflower oil, Tea]	High-risk; p=0.01
		7	Animal products (inverse)	[Animal protein, Animal fat, Cholesterol, Saturated fat, Monounsaturated fat, Soluble carbohydrates, Sodium, Calcium, Potassium, Phosphorus, Iron, Zinc, Thiamin, Riboflavin, Vitamin B6, Total folate, Niacin, Retinol, Vitamin D]	Protective; p<0.01
	Null				None
	Low				None

<sup>a</sup> General categories of dietary patterns. <sup>b</sup> Relates Supplemental Table 2 back to Supplemental Table 2. <sup>c</sup> Names bestowed by the authors. <sup>d</sup> Loadings include the foods and nutrients contributing to the dietary pattern with a factor loading coefficient of  $\geq 0.30$  (absolute value) with brackets [ ] indicating a negative contribution. <sup>e</sup> Summary of statistically significant results.

Supplemental Table 2: Results of Dietary Patterns and Breast Cancer Risk Publications (*continued*)

Category <sup>a</sup>	Risk	# <sup>b</sup>	Name <sup>c</sup>	Loadings <sup>d</sup>	Results <sup>e</sup>
Mediterranean (a priori)	High	23	Mediterranean	* Alcohol, Vegetables, Fruits, Legumes, Cereals, (MUFA+PUFA)/SFA, Dairy, Meat, Fish	Overall p=0.05; p=0.12 when excluding alcohol; among premenopausal and excluding alcohol p=0.05; p<0.05 for ER-/PR- tumors
		15	Mediterranean	*	All p>0.05
	Null	21	Mediterranean	*	All p>0.05 for pattern; but individual components a) vegetables, b) fish, and c) olive oil were significantly predictive
		28	Mediterranean	*	All p>0.05
	Low	9	Mediterranean	*	Protective; p=0.009; Individual components a) vegetables, b) legumes, and c) meat were significantly predictive
		29	Mediterranean	*	Protective; p=0.01; more predictive among postmenopausal
Healthy Eating Index (a priori)	High				None
	Null	29	Alternate Healthy Eating Index	* Oily fish, Leafy vegetables, Fruiting vegetables, Root vegetables, Other vegetables, Fruits, Nuts, Whole grains, Olives and other vegetable oils	All p>0.05
	Low	25	Healthy Eating Index	*	Protective; p=0.005 for premenopausal and postmenopausal (stratified); Individual components a) fruits protective for premenopausal and a) fruits, b) vegetables, and c) low saturated fat and d) sodium was protective for postmenopausal women

<sup>a</sup> General categories of dietary patterns. <sup>b</sup> Relates Supplemental Table 2 back to Supplemental Table 2. <sup>c</sup> Names bestowed by the authors. <sup>d</sup> Loadings include the foods and nutrients contributing to the dietary pattern with a factor loading coefficient of  $\geq 0.30$  (absolute value) with brackets [ ] indicating a negative contribution. <sup>e</sup> Summary of statistically significant results.

Supplemental Table 2: Results of Dietary Patterns and Breast Cancer Risk Publications (*continued*)

Category <sup>a</sup>	Risk	# <sup>b</sup>	Name <sup>c</sup>	Loadings <sup>d</sup>	Results <sup>e</sup>
Miscellaneous	High	14	High meat	Protein, Saturated fat, Monounsaturated fat, Linoleic acid, alpha-linolenic acid, cholesterol, and 3 heterocyclic amines	High-risk; p<0.0001; higher risk if positive family history
		16	Fatty cheese	Quattrolo cheese, High-fat cheese, Parma cheese, Raw vegetables, [Ricotta cheese]	High-risk; p<0.0001
	Null	2	Canteen	Cooked tomatoes, Other fruiting vegetables, Pulses, Pasta, Olive oil	All p>0.05
		17	Meat	Savory pastries, Beef, Chicken, Fried fish, Potato with fat	All p>0.05
		21	Meat/Potatoes	Red meat, Poultry, Deli meat, Potatoes, Sausage, Rabbit	All p>0.05
		21	Cereals/Milk/Dairy	Light yogurt, Low-fat cheese, Grains, Skim milk, Whole milk, Cheese,	All p>0.05
		24	Diet of the rich	Rice, Nuts, Egg, Chapati, Leguminous vegetables, Bread, Soda drinks, Red meat	All p>0.05
		24	Banana diet	Fish, Avocado, Banana, Green banana, Sugar, Watery fruits, Starchy tubers, Mbege, Pulses, Tea	All p>0.05
		28	Factor 1	Cheese, Crisps and savory snacks, Fresh fruit, Legumes, Low-fat milk, Nuts and seeds, Other fruit, Rice/pasta/other grains, Sauces, Vegetable mixed dishes, [Potatoes, Poultry, Red meat]	All p>0.05
		7	Vitamins and fiber	Vegetable protein, Soluble carbohydrates, Potassium, Phosphorus, Iron, Zinc, Thiamin, Riboflavin, Vitamin C, Vitamin B6, Total folate, Niacin, beta-Carotene, Vitamin E, Total fiber	All p>0.05
	Low	14	Antioxidants	Glucose, Fructose, Vitamin C, Vitamin E, Beta-carotene, Other carotenoids, Flavonoids, Sterols	Protective; p=0.001; more protective for postmenopausal women;
		16	Non alcohol beverages	Whole yogurt, Boiled eggs, Fried eggs, Total grains, Soft drinks, Tea, Yerba mate, [Beef]	Protective; p=0.02
		7	Unsaturated fats	Protective; p=0.03	Protective; p=0.03
		8	Dieter	High-fat dairy products, High-fat salad dressing, Cola beverages, Butter, Low-fat dairy, Margarine, Low-fat salad dressing, Low-fat high-sugar desserts, Diet beverages, Sugar substitutes	Protective; p=0.01 for premenopausal Hispanic women; p=0.04 for obese pre/perimenopausal

Supplemental Table 3: Diet History Questionnaire I Output Variables

Energy (kcal)	Vitamin A (IU)	Fatty Acid 4:0 (g)
Protein (g)	Vitamin A (mcg RE)	Fatty Acid 6:0 (g)
Fat (g)	Carotene (mcg RE)	Fatty Acid 8:0 (g)
Saturated Fat (g)	Vitamin E (mg)	Fatty Acid 10:0 (g)
Monounsaturated Fat (g)	Vitamin C (mg)	Fatty Acid 12:0 (g)
Polyunsaturated Fat (g)	Thiamin (mg)	Fatty Acid 14:0 (g)
Cholesterol (mg)	Riboflavin (mg)	Fatty Acid 16:0 (g)
Carbohydrate (g)	Niacin (mg)	Fatty Acid 16:1 (g)
Dietary Fiber (g)	Vitamin B6 (mg)	Fatty Acid 18:0 (g)
Alcohol (g)	Folate (mcg)	Fatty Acid 18:1 (g)
Total Dietary Fiber (g)	Vitamin B12 (mcg)	Fatty Acid 18:2 (g)
Insoluble Dietary Fiber (g)	Calcium (mg)	Fatty Acid 18:3 (g)
Soluble Dietary Fiber (g)	Phosphorus (mg)	Fatty Acid 18:4 (g)
Total grains (servings [s])	Magnesium (mg)	Fatty Acid 20:1 (g)
Whole grains (s)	Iron (mg)	Fatty Acid 20:4 (g)
Non-whole grains (s)	Zinc (mg)	Fatty Acid 20:5 (g)
Total vegetables (s)	Copper (mg)	Fatty Acid 22:1 (g)
Dark green vegetables (s)	Sodium (mg)	Fatty Acid 22:5 (g)
Deep yellow vegetables (s)	Potassium (mg)	Fatty Acid 22:6 (g)
Dry beans and peas (s)	Caffeine (mg)	Total Trans-fatty acids (g)
White potatoes (s)	Theobromine (mg)	Fatty Acid 16:1 Trans (g)
Starchy vegetables (s)	Selenium (mcg)	Fatty Acid 18:1 Trans (g)
Tomatoes (s)	Vitamin A, total activity (mcg RAE)	Fatty Acid 18:2 Trans (g)
Other vegetables (s)	Alpha-Carotene (mcg)	Discretionary fat (g)
Total fruits (s)	Beta-Carotene (mcg)	Added sugar (tsp)
Citrus, melons, berries (s)	Beta-Cryptoxanthin (mcg)	Alcohol (drinks)
Other fruits (s)	Lutein & Zeaxanthin (mcg)	Protein (%energy)
Total dairy (s)	Lycopene (mcg)	Carbohydrate (%energy)
Milk (s)	Beta-Carotene Equivalents (mcg)	Fat (%energy)
Yogurt (s)	Vitamin E (mg)	Saturated Fat (%energy)
Cheese (s)	Beta-Tocopherol (mg)	Monounsaturated Fat (%energy)
Total meat, poultry, fish (oz)	Delta-Tocopherol (mg)	Polyunsaturated Fat (%energy)
Beef, pork, lamb (oz)	Gamma-Tocopherol (mg)	Alcohol (%energy)
Organ meats (oz)	Vitamin D (mcg)	
Franks, luncheon (oz)	Methionine (g)	
Poultry (oz)	Folate (mcg)	
Fish, other seafood (oz)	Dietary Folate Equivalents (mcg)	
Eggs (oz)	Natural Folate (mcg)	
Soy products (oz)	Synthetic Folate (mcg)	
Nuts, seeds (oz)		

Supplemental Table 4: Comparison of Red Blood Cell Phospholipid  
Fatty Acid Composition by Evidence of Cytologic Atypia

Fatty acid	All	No Atypia	Atypia	P-value
6:0	0.015	0.015	0.014	0.92
8:0	0.024	0.025	0.021	0.38
10:0	0.011	0.011	0.010	0.60
11:0	0.010	0.012	0.0070	0.018
12:0	0.040	0.040	0.042	0.80
13:0	0.019	0.020	0.018	0.74
14:0	0.80	0.80	0.80	0.30
14:1	0.033	0.034	0.027	0.54
15:0	0.24	0.24	0.24	0.55
15:1n5	0.0070	0.0075	0.0060	0.43
16:0	22.3	22.0	23.0	0.26
16:0 DMA	0.96	1.13	0.89	0.06
16:1n7	0.47	0.47	0.46	0.79
17:1n5	0.055	0.055	0.055	0.96
18:0	18.3	17.4	18.7	0.075
18:0 DMA	2.47	2.47	2.42	0.98
18:1n9t	1.82	1.74	1.95	0.10
18:1n9c	12.1	12.0	12.2	0.67
18:1n7c	1.66	1.63	1.67	0.20
18:2n6t	0.058	0.062	0.057	0.96
18:2n6c	11.1	11.2	11.1	0.61
20:0	0.11	0.11	0.13	0.38
18:3n6	0.088	0.082	0.089	0.54
20:1n9	0.16	0.16	0.17	0.47
18:3n3	0.10	0.10	0.11	0.96
21:0	0.078	0.077	0.089	0.059
20:2n6	0.25	0.24	0.27	0.076
22:0	0.080	0.077	0.094	0.31
20:3n6	1.53	1.52	1.54	0.77
22:1n9	0.014	0.013	0.017	0.46
20:3n3	0.028	0.028	0.027	0.88
20:4n6 (AA)	14.4	14.5	13.9	0.054
22:2n6	0.023	0.024	0.020	0.23
24:0	0.16	0.16	0.17	0.44
20:5n3 (EPA)	0.49	0.55	0.48	0.097
24:1n9	0.12	0.12	0.12	0.99
22:4n6	2.77	2.74	2.91	0.28
22:5n6	0.49	0.47	0.50	0.70
22:5n3	1.72	1.77	1.64	0.13
22:6n3 (DHA)	4.20	4.46	3.98	0.05
N-3	6.71	7.11	6.20	0.031
N-6	30.5	31.0	29.7	0.18
EPA/AA	0.036	0.038	0.034	0.23
DHA/AA	0.29	0.30	0.27	0.13
EPA+DHA/AA	0.32	0.33	0.30	0.12
N-3/N-6	0.22	0.23	0.21	0.11

Median values are presented as weight percent of total fatty acids.

P-value calculated by Mann-Whitney U Test. DMA= dimethyl acetal

Supplemental Table 5: Comparison of Plasma Phospholipid  
Fatty Acid Composition by Evidence of Cytologic Atypia

Fatty acid	All	No Atypia	Atypia	P-value
6:0	0.014	0.016	0.013	0.72
8:0	0.022	0.021	0.030	0.62
10:0	0.0080	0.0090	0.0075	0.69
11:0	0.0070	0.0070	0.0070	0.31
12:0	0.033	0.034	0.033	0.92
13:0	0.013	0.014	0.012	0.59
14:0	0.70	0.74	0.66	0.37
14:1	0.025	0.028	0.022	0.024
15:0	0.24	0.24	0.24	0.69
15:1n5	0.006	0.0065	0.006	0.60
16:0	26.9	26.8	26.9	0.76
16:0 DMA	0.53	0.44	1.49	0.057
16:1n7	0.59	0.58	0.60	0.68
17:1n5	0.066	0.067	0.065	0.72
18:0	16.8	16.6	16.9	0.52
18:0 DMA	0.19	0.21	0.17	0.34
18:1n9t	1.57	1.57	1.63	0.78
18:1n9c	8.78	8.92	8.53	0.29
18:1n7c	1.56	1.56	1.60	0.80
18:2n6t	0.045	0.071	0.036	0.16
18:2n6c	21.4	21.4	21.4	0.94
20:0	0.10	0.10	0.093	0.22
18:3n6	0.13	0.16	0.11	0.20
20:1n9	0.12	0.12	0.12	0.19
18:3n3	0.15	0.16	0.13	0.064
21:0	0.086	0.094	0.073	0.0063
20:2n6	0.30	0.30	0.30	0.62
22:0	0.093	0.093	0.087	0.34
20:3n6	2.73	2.73	2.83	0.76
22:1n9	0.010	0.0095	0.011	0.97
20:3n3	0.019	0.020	0.017	0.25
20:4n6 (AA)	11.0	11.5	10.3	0.53
22:2n6	0.066	0.071	0.058	0.17
24:0	0.081	0.086	0.073	0.24
20:5n3 (EPA)	0.66	0.77	0.50	0.0079
24:1n9	0.075	0.076	0.073	0.51
22:4n6	0.34	0.34	0.34	0.89
22:5n6	0.22	0.23	0.22	0.85
22:5n3	0.69	0.72	0.61	0.20
22:6n3 (DHA)	3.24	3.39	3.18	0.164
N-3	4.93	5.07	4.54	0.027
N-6	35.8	35.6	36.2	0.86
EPA/AA	0.058	0.066	0.046	0.015
DHA/AA	0.29	0.31	0.28	0.19
EPA+DHA/AA	0.36	0.36	0.32	0.082
N-3/N-6	0.14	0.14	0.13	0.085

Median values are presented as weight percent of total fatty acids.

P-value calculated by Mann-Whitney U Test. DMA= dimethyl acetal

Supplemental Table 6: Comparison of Plasma Triacylglyceride  
Fatty Acid Composition by Evidence of Cytologic Atypia

Fatty acid	All	No Atypia	Atypia	P-value
6:0	0.021	0.021	0.021	0.59
8:0	0.034	0.036	0.033	0.60
10:0	0.026	0.029	0.018	0.24
11:0	0.019	0.02	0.019	0.97
12:0	0.23	0.19	0.27	0.09
13:0	0.035	0.038	0.030	0.47
14:0	1.93	2.00	1.84	0.40
14:1	0.13	0.14	0.10	0.33
15:0	0.29	0.32	0.27	0.13
15:1n5	0.015	0.014	0.018	0.43
16:0	24.4	24.4	24.1	0.69
16:0 DMA		not detectable		
16:1n7	2.57	2.58	2.49	0.43
17:1n5	0.21	0.21	0.20	0.28
18:0	4.34	4.46	4.12	0.18
18:0 DMA		not detectable		
18:1n9t	1.05	0.99	1.14	0.72
18:1n9c	30.9	30.9	30.9	0.23
18:1n7c	4.01	3.91	4.14	0.47
18:2n6t	0.18	0.19	0.15	0.079
18:2n6c	21.2	20.7	21.8	0.11
20:0	0.053	0.057	0.050	0.24
18:3n6	0.51	0.52	0.49	0.49
20:1n9	0.24	0.27	0.2	0.041
18:3n3	1.23	1.18	1.26	0.48
21:0	0.25	0.27	0.22	0.016
20:2n6	0.22	0.22	0.20	0.21
22:0	0.13	0.14	0.11	0.25
20:3n6	0.31	0.31	0.33	0.72
22:1n9	0.034	0.032	0.039	0.67
20:3n3	0.039	0.046	0.036	0.24
20:4n6 (AA)	1.49	1.56	1.42	0.11
22:2n6	0.031	0.033	0.030	0.21
24:0	0.032	0.035	0.028	0.60
20:5n3 (EPA)	0.19	0.27	0.14	0.018
24:1n9	0.023	0.024	0.023	0.94
22:4n6	0.17	0.17	0.15	0.61
22:5n6	0.10	0.11	0.082	0.11
22:5n3	0.24	0.26	0.12	0.048
22:6n3 (DHA)	0.34	0.38	0.28	0.018
N-3	2.17	2.37	1.96	0.041
N-6	24.5	24.0	25.0	0.20
EPA/AA	0.12	0.14	0.099	0.037
DHA/AA	0.23	0.25	0.20	0.14
EPA+DHA/AA	0.37	0.41	0.31	0.053
N-3/N-6	0.093	0.11	0.083	0.014

Median values are presented as weight percent of total fatty acids.

P-value calculated by Mann-Whitney U Test. DMA= dimethyl acetal



Supplemental Table 7: Comparison of Breast Phospholipid  
Fatty Acid Composition by Evidence of Cytologic Atypia

Fatty acid	All	No Atypia	Atypia	P-value
6:0	0.017	0.017	0.015	0.49
8:0	0.020	0.018	0.020	0.83
10:0	0.028	0.022	0.038	0.12
11:0	0.023	0.021	0.031	0.069
12:0	0.12	0.11	0.14	0.41
13:0	0.057	0.058	0.055	0.88
14:0	3.03	3.05	2.97	0.13
14:1	0.14	0.14	0.14	0.32
15:0	0.69	0.69	0.78	0.34
15:1n5	0.014	0.016	0.014	0.89
16:0	32.5	32.6	32.0	0.031
16:0 DMA	0.073	0.047	0.080	0.24
16:1n7	1.29	1.32	1.24	0.083
17:1n5	0.19	0.19	0.20	0.95
18:0	32.9	33.1	32.8	0.81
18:0 DMA	0.047	0.034	0.055	0.71
18:1n9t	7.38	7.46	7.16	0.49
18:1n9c	14.3	14.4	14.3	0.54
18:1n7c	1.40	1.40	1.37	0.83
18:2n6t	0.20	0.18	0.21	0.6
18:2n6c	2.00	1.90	2.20	0.14
20:0	0.29	0.29	0.32	0.049
18:3n6	0.047	0.050	0.043	0.57
20:1n9	0.12	0.11	0.19	0.25
18:3n3	0.03	0.034	0.029	0.67
21:0	0.19	0.19	0.20	0.36
20:2n6	0.039	0.032	0.047	0.22
22:0	0.11	0.10	0.13	0.085
20:3n6	0.18	0.17	0.21	0.53
22:1n9	0.054	0.063	0.037	0.65
20:3n3	0.023	0.021	0.025	0.36
20:4n6 (AA)	0.72	0.62	0.93	0.28
22:2n6	0.054	0.054	0.056	0.28
24:0	0.14	0.14	0.15	0.39
20:5n3 (EPA)	0.055	0.055	0.062	0.95
24:1n9	0.036	0.027	0.041	0.2
22:4n6	0.14	0.12	0.18	0.65
22:5n6	0.054	0.044	0.068	0.67
22:5n3	0.10	0.085	0.13	0.24
22:6n3 (DHA)	0.25	0.25	0.27	0.77
N-3	0.49	0.52	0.47	0.77
N-6	4.25	4.05	4.54	0.63
EPA/AA	0.080	0.10	0.071	0.58
DHA/AA	0.23	0.26	0.20	0.36
EPA+DHA/AA	0.34	0.36	0.28	0.37
N-3/N-6	0.12	0.13	0.12	0.44

Median values are presented as weight percent of total fatty acids.

P-value calculated by Mann-Whitney U Test. DMA= dimethyl acetal

Supplemental Table 8: Comparison of Breast Triacylglyceride  
Fatty Acid Composition by Evidence of Cytologic Atypia

Fatty acid	All	No Atypia	Atypia	P-value
6:0	0.018	0.016	0.021	0.68
8:0	0.019	0.020	0.012	0.25
10:0	0.029	0.028	0.030	0.68
11:0	0.013	0.013	0.014	0.61
12:0	0.39	0.39	0.43	0.66
13:0	0.024	0.026	0.018	0.23
14:0	2.49	2.51	2.34	0.52
14:1	0.19	0.19	0.18	0.56
15:0	0.31	0.31	0.30	0.77
15:1n5	0.012	0.011	0.014	0.95
16:0	21.0	21.2	20.3	0.11
16:0 DMA		not detectable		
16:1n7	2.76	2.78	2.74	0.68
17:1n5	0.19	0.19	0.19	0.84
18:0	6.71	6.71	6.86	0.72
18:0 DMA		not detectable		
18:1n9t	2.00	2.11	1.89	0.79
18:1n9c	37.4	37.3	38.2	0.41
18:1n7c	4.14	4.05	4.17	0.99
18:2n6t	0.26	0.25	0.26	0.77
18:2n6c	16.6	16.2	17.1	0.089
20:0	0.15	0.15	0.16	0.44
18:3n6	0.075	0.078	0.070	0.16
20:1n9	0.61	0.61	0.62	0.77
18:3n3	0.78	0.81	0.73	0.65
21:0	0.25	0.25	0.25	0.55
20:2n6	0.28	0.30	0.27	0.91
22:0	0.037	0.050	0.032	0.79
20:3n6	0.24	0.28	0.20	0.11
22:1n9	0.044	0.049	0.041	0.19
20:3n3	0.030	0.030	0.029	0.72
20:4n6 (AA)	0.32	0.36	0.26	0.23
22:2n6	0.028	0.028	0.027	0.91
24:0	0.029	0.033	0.023	0.81
20:5n3 (EPA)	0.035	0.048	0.030	0.15
24:1n9	0.022	0.022	0.025	0.91
22:4n6	0.19	0.21	0.16	0.21
22:5n6	0.032	0.038	0.027	0.46
22:5n3	0.12	0.13	0.075	0.036
22:6n3 (DHA)	0.087	0.090	0.057	0.12
N-3	1.13	1.18	1.04	0.11
N-6	18.3	17.8	18.6	0.25
EPA/AA	0.11	0.12	0.092	0.77
DHA/AA	0.22	0.22	0.22	0.84
EPA+DHA/AA	0.37	0.37	0.41	0.58
N-3/N-6	0.064	0.065	0.053	0.018

Median values are presented as weight percent of total fatty acids.

P-value calculated by Mann-Whitney U Test. DMA= dimethyl acetal

Supplemental Table 9: Raw Output of the DHQ-I		
	<u>Atypia (n=23)</u>	<u>No Atypia (n=42)</u>
	Mean±STD (Range)	
Energy intake (Kcal/day)	1382±479 (687-2413)	1384±401 (755-2176)
Carbohydrate (% of energy)	52.1±7.0 (41-68)	47.4±10.0 (16-63)
Protein (% of energy)	16.7±2.4 (12-20)	17.8±2.6 (13-27)
Fat (% of energy)	32.2±5.2 (23-42)	33.0±7.8 (18-54)
Daily alcohol intake (g/day)	2.9±4.1 (0.0-18)	9.1±15.2 (0.0-77)
<u>Average Servings per Day of USDA Pyramid Food Groups</u>		
All Grains	3.6±1.7 (1.3-7.3)	3.3±1.2 (0.8-5.3)
Whole Grains	0.87±0.67 (0.1-2.4)	0.80±0.47 (0.1-2.4)
Refined Grains	2.7±1.1 (1.1-5.0)	2.5±0.94 (0.7-4.2)
All Vegetables	3.3±1.9 (1.1-8.1)	4.0±2.5 (1.1-11.1)
Dark Green Vegetables	0.41±0.52 (0.03-2.0)	0.58±0.55 (0.02-2.0)
Deep Yellow Vegetables	0.31±0.41 (0.02-1.7)	0.28±0.26 (0.02-1.1)
Beans and Peas	0.11±0.09 (0.01-0.44)	0.12±0.17 (0.01-1.0)
White Potatoes	0.45±0.28 (0.11-1.1)	0.41±0.38 (0.02-1.7)
Other Starchy Vegetables	0.27±0.18 (0.06-0.94)	0.30±0.30 (0.02-1.6)
Tomatoes	0.40±0.31 (0.13-1.3)	0.44±0.33 (0.12-1.6)
Other Vegetables	1.3±1.1 (0.28-4.9)	1.9±1.5 (0.3-6.4)
All Fruits	2.2±1.6 (0.13-7.1)	1.7±1.2 (0.15-5.1)
Melons, Berries and Citrus	0.82±0.66 (0.04-3.0)	0.72±0.69 (0.05-3.1)
Other Fruits	1.4±1.1 (0.09-4.1)	0.97±0.90 (0.07-4.7)
All Dairy	1.4±1.2 (0.30-4.6)	1.3±0.69 (0.21-3.1)
Milk	0.83±0.97 (0.05-3.2)	0.69±0.63 (0.03-2.8)
Yogurt	0.15±0.21 (0.01-0.80)	0.21±0.23 (0.00-0.80)
Cheese	0.39±0.32 (0.03-1.4)	0.38±0.28 (0.03-1.2)
All Meats	2.9±1.3 (0.71-5.1)	3.1±1.7 (0.38-7.2)
Beef, Pork, and Lamb	1.1±0.49 (0.23-2.3)	1.1±0.70 (0.15-3.3)
Processed Meat	0.44±0.55 (0.02-1.8)	0.36±0.40 (0.0-2.0)
Poultry	1.1±0.71 (0.13-2.9)	1.2±0.89 (0.05-4.0)
Fish	0.30±0.29 (0.01-0.86)	0.51±0.68 (0.01-3.8)
Eggs	0.27±0.22 (0.02-0.78)	0.22±0.19 (0.02-1.2)
Soy	0.02±0.032 (0.00-0.11)	0.02±0.035 (0.00-0.16)
Nuts	0.25±0.18 (0.02-0.61)	0.38±0.42 (0.03-1.7)

Supplemental Table 10: Survey items that contribute the greatest to USDA pyramid food groups are presented in the top-left. Magnitude of contribution decreases from top to bottom, then left to right.

Supplemental Table 10: Item Response Contributions to U.S.D.A. Food Groups			
Whole Grains	Refined Grains		
Popcorn	Pasta	Beef meatball or meatloaf	Vegetable medley
Breakfast cereal	Pizza	Egg roll	Fruit drink
Hot breakfast cereal	Pretzel	Creamed soup	Miscellaneous syrup
Rice milk	Macaroni and cheese	Meal replacement bar	Sour cream
Whole grain bread	Lasagna, ravioli, or shells	Meal replacement liquid	Shortribs or spareribs
Granola bar	Stuffing or dumpling	Hot breakfast cereal	Coleslaw
Potato or corn chips	Pancake, waffle, or french toast	Cheesecake	Plantain
Pancakes, waffles, or french toast	Fruit pie	Fried chicken	
Muffin	Fruit crisp or cobbler	Pudding or custard	
Rice	Cornbread	Soups with vegetables	
English muffin or bagel	Rice	Gravy	
Meal replacement bar	Mexican mixture	Beef steak	
Crackers	Croissant	Chili	
Tofu	White bread	Soups with beans	
Mexican mixture	Chow mein noodle	Pork	
Cheesecake	Biscuit	Fish or oyster	
Cream or custard pie	Bagel	Diet mayonnaise	
Cookie or brownie	Donut, sweet roll, danish, or pop tarts	Candy (not chocolate)	
Soup with rice or noodles	Cream or custard pie	Veal, venison, or lamb	
Chicken mixture	Pasta salad	White sauce	
Soups with beans	Muffins or dessert bread	Ice cream	
Soups with vegetables	Pumpkin or sweet potato pie	Liverwurst	
Cornbread	Fried fish	Granola bar	
Lasagna, ravioli, or shells	Soup with rice or noodles	Cheese sauce	
Biscuit	Cracker	Beans	
	Cake	Chocolate candy	
	Chicken mixture	Fat-free mayonnaise	
	Beef stew, pot pie, or mixture	Frozen yogurt or sorbet	
	Potato or corn chips	Low-fat salad dressing	
	Breakfast cereal	Milkshake	
	Cookie or brownie	Tofu	
	Ground chicken or turkey	Potato salad	

<i>(continued)</i> Supplemental Table 10: Item Response Contributions to U.S.D.A. Food Groups				
<b>Dark Green Vegetables</b>	<b>Deep Yellow Vegetables</b>	<b>Beans</b>	<b>Potato</b>	
Broccoli Spinach or greens Vegetable medley	Sweet potato Carrots Vegetable medley Beef stew, pot pie, or mixture Pumpkin or sweet potato pie Soups with vegetables Coleslaw Soups with beans Chicken mixture Soups with ride or noodles Pasta salad Other vegetables Red pasta sauce	Beans Soups with beans Chili Mexican mixture Tofu	White potato Potato salad Fried potato Potato or corn chips Beef stew, pot pie, or mixtures Creamed soup	
<b>Starchy Veg</b>	<b>Tomato</b>			
Corn Peas Vegetable medley Soups with vegetables Beef stew, pot pie, or mixture Beans Chicken mixture Tea Creamed soup Other vegetables Soups with rice or noodles Pasta salad	Tomato juice Chili Lasagna, Ravioli, or Shells Pasta with red sauce Raw tomatoes Pizza Salsa Soups with vegetables Tofu Ketchup Beef stew, pot pie, or mixture Creamed soup	Mexican mixture Beef meatball or meatloaf Vegetable medley Beans Chicken mixture Soups with beans Soups with rice or noodles Shortribs or spareribs Guacamole or avocado		

(continued) Supplemental Table 10: Item Response Contributions to U.S.D.A. Food Groups			
Other Vegetables		Citrus, Melons, and Berries	Other Fruit
String beans Cabbage Cauliflower Brussel sprouts Lettuce Coleslaw Other vegetables Pasta salad Vegetable medley Hot peppers Beef stew, pot pie, or mixture Soups with vegetables Meat sauce for pasta Pickled vegetables or fruit Chili Potato salad Peppers Mexican mixture Chicken mixture Onion Olives	Egg roll Soups with beans Pizza Meatballs or meatloaf Soups with rice or noodles Beans Rice Tomato salsa Creamed soup Lasagna, Ravioli, or Shells Ketchup Stuffing or Dumpling Peas Liverwurst Pasta Non-fat salad dressing Tofu Fried Potato Fat-free mayonnaise Sour cream Salad dressing	Other melon Cantaloupe Orange or grapefruit juice Orange Grapefruit Strawberries Fruit drink Fruit salad Other juice Fruit crisp or cobbler Yogurt Fruit pie Cake Muffins or dessert bread	Plantain Grape Apple sauce Other juice Apple Pear Fruit crisp or cobbler Peach, nectarine, or plum Banana Dried fruit Fruit salad Guacamole or avocado Apricot Fruit pie Gelatin
Milk			
Milk Milkshake Meal replacement liquid Creamed soup Frozen yogurt or sorbet Ice cream Pudding or custard Egg substitutes Pumpkin or sweet potato pie Macaroni and cheese Gravy	Cream or custard pie White sauce Cheese sauce Chocolate candy Hot breakfast cereal Beef meatball or meatloaf Heavy cream or half-and-half Pasta Chicken mixture Salad dressing Soups with vegetables	Meat sauce or pasta Beef stew, pot pie, or mixture Miscellaneous syrup Meal replacement bar Non-fat salad dressing Pancake, waffle, or french Toast Biscuit White potato Whipped cream Fried fish	Yogurt

<i>(continued)</i> Supplemental Table 10: Item Response Contributions to U.S.D.A. Food Groups				
<b>Cheese</b>	<b>Beef, Pork, and Lamb</b>	<b>Processed Meat</b>	<b>Poultry</b>	<b>Fish</b>
Lasagna	Steak	Hot dog	Chicken	Fish
Pizza	Roast beef	Sausage	Fried chicken	Tuna
Cheese	Beef stew, pot pie, or mixture	Cold cuts	Turkey	Fried fish
Macaroni and cheese	Beef burger	Lunch meat	Chicken mixture	Fish or oyster
Mexican mixture	Veal, venison, or lamb	Liverwurst	Ground turkey or chicken	Creamed soup
Cottage or Ricotta cheese	Ham	Pizza		
Cheesecake	Beef meatball or meatloaf	Gravy		
Cheese sauce	Pork	Lasagna, ravioli, or shells		
Cream sauce	Chili	Croissant		
Croissant	Meat sauce for pasta			
	Mexican mixture			
	Lasagna, ravioli, or shells			
	Soups with vegetables			
	Bacon			
	Cold cuts			
	Canadian bacon			
	Soups with beans			
	Egg roll			
	Macaroni and cheese			
	Soup with rice or noodles			
	Croissant			
	Pizza			
	Gravy			
	Stuffing or Dumpling			

<i>(continued)</i> Supplemental Table 10: Item Response Contributions to U.S.D.A. Food Groups				
<b>Eggs</b>			<b>Soy</b>	
Egg	Egg Roll	Diet Mayonnaise	Tofu	
Egg substitute	Pasta salad	Rice	Soy milk	
Egg salad	Cream or custard pie	Soups with noodles or rice		
Pecan pie	Beef meatball or meatloaf	Chicken mixture		<b>Nuts</b>
Potato salad	Pudding or custard	Milkshake	Whole nuts or seeds	Candy (not chocolate)
Pumpkin or sweet potato pie	Fish or oysters	Fish	Nut or seed butter	Breakfast cereal
Fried fish	Mayonnaise	Macaroni and cheese	Pecan pie	Crackers
Croissant	Mexican mixture	Liverwurst	Chocolate candy	Fruit salad
Meat sauce for pasta	Pork	Fried chicken	Granola bar	Cookie or Brownie
Lasagna, ravioli, or shells	Coleslaw	Stuffing or dumpling	Cream or custard pie	Pasta
Pancake, waffle, or french toast	Veal, Venison, or Lamb		Meal replacement bar	
<b>Added Sugar</b>				
Pecan pie	Meal replacement liquid	Yogurt	Popcorn	Chili
Maple syrup	Chocolate candy	Granola bar	Pancake, waffle, or french toast	Wine
Soft drink	Fruit pie	Jam or jelly	Whipped cream	Whole grain bread
Milkshake	Pudding or custard	Pasta salad	Lasagna, ravioli, or shells	Pickled vegetables or fruit
Fruit drink	Donut, sweet roll, danish, or pop tarts	Salad dressing	Ketchup	Cottage or ricotta cheese
Cakes	Gelatin	Peach, nectarine, or plum	Croissants	Beef meatball or meatloaf
Fruit crisp or cobbler	Cookie or brownie	Pear	Mayonnaise	Creamed soup
Candy (not chocolate)	Meal replacement bar	Fruit salad	Coleslaw	Shortribs or spare ribs
Cream or custard pie	Pumpkin or sweet potato pie	Cornbread	Crackers	Chicken mixture
Miscellaneous syrup	Breakfast cereal	Meat sauce or pasta	White bread	
Ice cream	Applesauce	Beans	Biscuit	
Frozen yogurt or sorbet	Muffin or dessert bread	Potato salad	Soup with noodles or rice	
Cheesecake	Sugar or honey		Stuffing or dumpling	



Supplemental Table 11: High-Fat-Meat-Low-Carb Dietary Pattern			
<u>Positive (+) Loading</u>		<u>Negative (-) Loading</u>	
Dietary Variable	$\lambda$ (+)	Dietary Variable	$\lambda$ (-)
Fat (%)	0.84	Carbohydrate (%)	0.80
Monounsaturated Fat (%)	0.82	Milk	0.56
Saturated Fat (%)	0.77	Vitamin C	0.53
FA 16:1	0.58	Folate (dietary equivalents)	0.53
MUFA (g)	0.56	Folic acid	0.52
FA 18:1	0.55	Vitamin A (retinoid equivalents)	0.49
FA 18:0	0.50	Vitamin A (activity)	0.49
FA 16:0	0.50	Theophylline	0.49
Polyunsaturated Fat (%)	0.50	Folate	0.48
Trans 16:1	0.49	Carbohydrates (g)	0.44
Saturated Fat (g)	0.49	Fruit	0.43
Fat (g)	0.48	Vitamin B6	0.42
Trans 18:1	0.48	Vitamin A	0.42
Added fat	0.48	Potassium	0.39
Trans fat	0.47	Glycemic Load	0.39
FA 20:1	0.47	Riboflavin	0.38
Total Meat	0.45	Other fruit	0.38
Processed Meat	0.42	Iron	0.38
Trans 18:2	0.42	Thiamin	0.38
Cheese	0.40	Beta-Carotene	0.38
14:0	0.40	Beta-carotene (equivalents)	0.37
20:4	0.40	Lutein and Zeaxanthin	0.36
Cholesterol	0.40	Soy	0.36
Red Meat	0.39	Added sugar	0.35
Alcohol (%)	0.38	Insoluble fiber	0.35
Alcoholic drinks	0.38	Dark green vegetables	0.34
Alcohol (g)	0.38	Vitamin D	0.34
FA 18:3	0.37	Carotene	0.34
FA 6:0	0.34	Soluble fiber	0.33
Gamma-Tocopherol	0.32	Copper	0.33
Polyunsaturated fat (g)	0.31	Folate (food)	0.33
FA 18:2	0.31	Magnesium	0.33
FA 4:0	0.30	Dairy	0.32
		Calcium	0.32
		Citrus, Melons, and berries	0.31
		Fiber	0.31

**Supplemental Table 12:** N=62 for plasma phospholipids, plasma triacylglycerides, and erythrocyte phospholipids. N=32 for breast adipose triacylglycerides. \*By simple logistic regression, only the concentration of EPA in plasma phospholipids was significantly predictive of atypia status; a Z-score (0.43%) increase was associated with 64% lower odds of atypia (OR 95% CI: 0.25 to 0.85).

Supplemental Table 12: Tissue concentration of fatty acids as weight percent						
Lipid Compartment	Class	Fatty Acid	Atypia (N=22)		No Atypia (N=40)	
			Mean $\pm$ STD	Range	Mean $\pm$ STD	Range
Plasma Phospholipids	Mono	Oleic 18:1n9c	8.7 $\pm$ 1.7	5.8 - 11.7	9.0 $\pm$ 1.3	6.6 - 13.1
		Alpha-linolenic 18:3n3	0.14 $\pm$ 0.06	0.033 - 0.30	0.19 $\pm$ 0.09	0.075 - 0.40
	N-3 PUFA	Eicosapentaenoic 20:5n3	0.58 $\pm$ 0.27*	0.16 - 1.04	0.87 $\pm$ 0.46*	0.24 - 2.21
		Docosahexaenoic 22:6n3	3.0 $\pm$ 1.1	1.6 - 5.9	3.6 $\pm$ 1.2	1.6 - 6.6
	N-6 PUFA	Linoleic 18:2n6c	21.2 $\pm$ 3.6	11.7 - 27.4	21.3 $\pm$ 4.0	12.2 - 31.7
		Arachidonic 20:4n6	10.6 $\pm$ 2.3	4.0 - 14.6	11.0 $\pm$ 2.3	6.1 - 17.0
	Trans	Elaidic 18:1n9t	1.7 $\pm$ 0.5	0.55 - 2.5	1.6 $\pm$ 0.5	0.44 - 2.9
		Linolelaidic 18:2n6t	0.087 $\pm$ 0.112	0.022 - 0.52	0.082 $\pm$ 0.078	0.011 - 0.46
	Mono	Oleic 18:1n9c	30.5 $\pm$ 4.7	16.7 - 39.1	31.9 $\pm$ 3.9	22.4 - 40.8
		Alpha-linolenic 18:3n3	1.3 $\pm$ 0.46	0.65 - 2.5	1.2 $\pm$ 0.59	0.28 - 3.8
Plasma Triacylglycerides	N-3 PUFA	Eicosapentaenoic 20:5n3	0.32 $\pm$ 0.71	0.016 - 3.4	0.38 $\pm$ 0.39	0.021 - 1.9
		Docosahexaenoic 22:6n3	0.39 $\pm$ 0.40	0.091 - 1.8	0.50 $\pm$ 0.37	0.043 - 2.1
	N-6 PUFA	Linoleic 18:2n6c	21.5 $\pm$ 5.0	8.8 - 30.6	20.1 $\pm$ 4.0	13.3 - 28.2
		Arachidonic 20:4n6	1.4 $\pm$ 0.47	0.79 - 2.6	1.7 $\pm$ 0.61	0.67 - 3.3
	Trans	Elaidic 18:1n9t	1.1 $\pm$ 0.42	0.49 - 1.9	1.2 $\pm$ 0.72	0.17 - 3.3
		Linolelaidic 18:2n6t	0.17 $\pm$ 0.082	0.027 - 3.8	0.24 $\pm$ 0.19	0.024 - 1.1

(continued) Supplemental Table 12: Tissue concentration of fatty acids as weight percent						
Lipid Compartment	Class	Fatty Acid	Atypia (N=22)		No Atypia (N=40)	
			Mean ± STD	Range	Mean ± STD	Range
Red Blood Cell Phospholipids	Mono	Oleic 18:1n9c	12.0 ± 1.2	9.5 - 14.1	12.1 ± 1.0	10.4 - 15.2
		Alpha-Linolenic 18:3n3	0.15 ± 0.16	0.046 - 0.85	0.13 ± 0.075	0.060 - 0.41
	N-3 PUFA	Eicosapentaenoic 20:5n3	0.53 ± 0.31	0.20 - 1.5	0.69 ± 0.51	0.23 - 3.1
		Docosahexaenoic 22:6n3	3.9 ± 1.7	1.6 - 9.8	4.6 ± 1.3	2.4 - 7.6
	N-6 PUFA	Linoleic 18:2n6c	10.9 ± 1.4	8.5 - 13.7	11.1 ± 1.9	6.9 - 15.1
		Arachidonic 20:4n6	13.7 ± 2.1	9.7 - 18.8	14.6 ± 2.1	8.5 - 18.3
	<i>Trans</i>	Elaidic 18:1n9t	2.0 ± 0.64	0.51 - 3.2	1.8 ± 0.68	0.47 - 4.3
		Linolelaidic 18:2n6t	0.12 ± 0.17	0.014 - 0.86	0.12 ± 0.21	0.015 - 1.0
Breast Adipose Triacylglycerides	Mono	Oleic 18:1n9c	39.9 ± 3.8	34.6 - 45.5	36.8 ± 4.3	21.4 - 42.3
		Alpha-Linolenic 18:3n3	0.65 ± 0.32	0.046 - 0.95	0.78 ± 0.27	0.027 - 1.3
	N-3 PUFA	Eicosapentaenoic 20:5n3	0.033 ± 0.015	0.015 - 0.060	0.095 ± 0.18	0.006 - 0.92
		Docosahexaenoic 22:6n3	0.089 ± 0.069	0.035 - 0.18	0.12 ± 0.085	0.048 - 0.42
	N-6 PUFA	Linoleic 18:2n6c	17.3 ± 2.3	14.2 - 21.0	15.7 ± 2.6	10.2 - 21.4
		Arachidonic 20:4n6	0.39 ± 0.21	0.20 - 0.70	0.42 ± 0.25	0.19 - 1.4
	<i>Trans</i>	Elaidic 18:1n9t	2.0 ± 0.58	1.3 - 2.9	2.2 ± 0.78	0.92 - 4.4
		Linolelaidic 18:2n6t	0.25 ± 0.028	0.22 - 0.29	0.28 ± 0.17	0.13 - 1.0

Supplemental Table 13: Interactions between Menopause, Age, and BMI and Dietary Patterns										
Dietary Pattern	AUC <sup>b</sup>	Overall <sup>c</sup>	P-value <sup>a</sup>							
			Menopause				Age		BMI	
			Pre-	Post-	Interaction	≤49yrs	≥50yrs	Interaction	Normal	≥25
Energy	0.54	0.48	0.11	0.59	0.12	0.55	0.86	0.83	0.96	0.34
Fat-Alcohol-Meat	0.53	0.78	0.51	0.76	0.51	0.70	0.40	0.37	0.25	0.08
Traditional/Modern	0.67	0.01	0.01	0.35	0.31	0.003	0.83	0.05	0.17	0.02
										0.25

Supplemental Table 13:

<sup>a</sup> P-values were computed by the likelihood ratio test using logistic regression. P-values are presented for interactions and from stratified analyses performed on premenopausal, postmenopausal, <50yrs old, ≥50yrs old, normal BMI, and overweight/obese participants.

<sup>b</sup> The area-under-the-curve (AUC) statistic is derived from the receiver-operator-characteristic curve for the entire sample. It represents ability of a continuous variable (dietary characteristic) to accurately discriminate between two states (atypia versus no atypia); a value of “0.5” indicates a 50/50 chance, with “1” meaning the continuous variable categorizes individuals with 100% accuracy.

<sup>c</sup> P-value derived from likelihood ratio test using the entire sample in a simple logistic regression model with the dietary pattern as a continuous variable.

## Appendix 1: Diet History Questionnaire I

NATIONAL INSTITUTES OF HEALTH

### *Diet History Questionnaire*



#### GENERAL INSTRUCTIONS

- Answer each question as best you can. Estimate if you are not sure. A guess is better than leaving a blank.
- Use only a black ball-point pen. Do not use a pencil or felt-tip pen. Do not fold, staple, or tear the pages.
- Put an X in the box next to your answer.
- If you make any changes, cross out the incorrect answer and put an X in the box next to the correct answer. Also draw a circle around the correct answer.
- If you mark NEVER, NO, or DON'T KNOW for a question, please follow any arrows or instructions that direct you to the next question.

BEFORE TURNING THE PAGE, PLEASE COMPLETE THE FOLLOWING QUESTIONS.

Today's date:

MONTH	DAY	YEAR
<input type="checkbox"/> Jan	<input type="checkbox"/> 0 <input type="checkbox"/> 0	<input type="checkbox"/> 2007
<input type="checkbox"/> Feb	<input type="checkbox"/> 0 <input type="checkbox"/> 0	<input type="checkbox"/> 2008
<input type="checkbox"/> Mar	<input type="checkbox"/> 1 <input type="checkbox"/> 1	<input type="checkbox"/> 2009
<input type="checkbox"/> Apr	<input type="checkbox"/> 2 <input type="checkbox"/> 2	<input type="checkbox"/> 2010
<input type="checkbox"/> May	<input type="checkbox"/> 3 <input type="checkbox"/> 3	<input type="checkbox"/> 2011
<input type="checkbox"/> Jun	<input type="checkbox"/> 3 <input type="checkbox"/> 3	
<input type="checkbox"/> Jul	<input type="checkbox"/> 4 <input type="checkbox"/> 4	
<input type="checkbox"/> Aug	<input type="checkbox"/> 5 <input type="checkbox"/> 5	
<input type="checkbox"/> Sep	<input type="checkbox"/> 6 <input type="checkbox"/> 6	
<input type="checkbox"/> Oct	<input type="checkbox"/> 7 <input type="checkbox"/> 7	
<input type="checkbox"/> Nov	<input type="checkbox"/> 8 <input type="checkbox"/> 8	
<input type="checkbox"/> Dec	<input type="checkbox"/> 9 <input type="checkbox"/> 9	

In what month were you born?

<input type="checkbox"/> Jan
<input type="checkbox"/> Feb
<input type="checkbox"/> Mar
<input type="checkbox"/> Apr
<input type="checkbox"/> May
<input type="checkbox"/> Jun
<input type="checkbox"/> Jul
<input type="checkbox"/> Aug
<input type="checkbox"/> Sep
<input type="checkbox"/> Oct
<input type="checkbox"/> Nov
<input type="checkbox"/> Dec

In what year were you born?

19	<input type="checkbox"/> 0 <input type="checkbox"/> 0
	<input type="checkbox"/> 1 <input type="checkbox"/> 1
	<input type="checkbox"/> 2 <input type="checkbox"/> 2
	<input type="checkbox"/> 3 <input type="checkbox"/> 3
	<input type="checkbox"/> 4 <input type="checkbox"/> 4
	<input type="checkbox"/> 5 <input type="checkbox"/> 5
	<input type="checkbox"/> 6 <input type="checkbox"/> 6
	<input type="checkbox"/> 7 <input type="checkbox"/> 7
	<input type="checkbox"/> 8 <input type="checkbox"/> 8
	<input type="checkbox"/> 9 <input type="checkbox"/> 9

Are you male or female?

<input type="checkbox"/> Male
<input type="checkbox"/> Female

BAR CODE LABEL OR SUBJECT ID  
HERE

1. Over the past 12 months, how often did you drink **tomato juice** or **vegetable juice**?

☐ NEVER (GO TO QUESTION 2)

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2–3 times per month      | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 1–2 times per week       | <input type="checkbox"/> 4–5 times per day       |
| <input type="checkbox"/> 3–4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week       |  |

- 1a. Each time you drank **tomato juice** or **vegetable juice**, how much did you usually drink?

- ☐ Less than ¼ cup (6 ounces)  
☐ ¼ to 1¼ cups (6 to 10 ounces)  
☐ More than 1¼ cups (10 ounces)

2. Over the past 12 months, how often did you drink **orange juice** or **grapefruit juice**?

☐ NEVER (GO TO QUESTION 3)

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2–3 times per month      | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 1–2 times per week       | <input type="checkbox"/> 4–5 times per day       |
| <input type="checkbox"/> 3–4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week       |  |

- 2a. Each time you drank **orange juice** or **grapefruit juice**, how much did you usually drink?

- ☐ Less than ¼ cup (6 ounces)  
☐ ¼ to 1¼ cups (6 to 10 ounces)  
☐ More than 1¼ cups (10 ounces)

3. Over the past 12 months, how often did you drink **other 100% fruit juice** or **100% fruit juice mixtures** (such as apple, grape, pineapple, or others)?

☐ NEVER (GO TO QUESTION 4)

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2–3 times per month      | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 1–2 times per week       | <input type="checkbox"/> 4–5 times per day       |
| <input type="checkbox"/> 3–4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week       |  |

- 3a. Each time you drank **other fruit juice** or **fruit juice mixtures**, how much did you usually drink?

- ☐ Less than ¼ cup (6 ounces)  
☐ ¼ to 1½ cups (6 to 12 ounces)  
☐ More than 1½ cups (12 ounces)

Question 4 appears in the next column

Over the past 12 months...

4. How often did you drink other **fruit drinks** (such as cranberry cocktail, Hi-C, lemonade, or Kool-Aid, diet or regular)?

☐ NEVER (GO TO QUESTION 5)

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2–3 times per month      | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 1–2 times per week       | <input type="checkbox"/> 4–5 times per day       |
| <input type="checkbox"/> 3–4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week       |  |

- 4a. Each time you drank **fruit drinks**, how much did you usually drink?

- ☐ Less than 1 cup (8 ounces)  
☐ 1 to 2 cups (8 to 16 ounces)  
☐ More than 2 cups (16 ounces)

- 4b. How often were your fruit drinks **diet** or **sugar-free drinks**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

5. How often did you drink **milk as a beverage** (NOT in coffee, NOT in cereal)? (Please include chocolate milk and hot chocolate.)

☐ NEVER (GO TO QUESTION 6)

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2–3 times per month      | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 1–2 times per week       | <input type="checkbox"/> 4–5 times per day       |
| <input type="checkbox"/> 3–4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week       |  |

- 5a. Each time you drank **milk as a beverage**, how much did you usually drink?

- ☐ Less than 1 cup (8 ounces)  
☐ 1 to 1½ cups (8 to 12 ounces)  
☐ More than 1½ cups (12 ounces)

- 5b. What kind of **milk** did you usually drink?

- ☐ Whole milk  
☐ 2% fat milk  
☐ 1 % fat milk  
☐ Skim, nonfat, or ½% fat milk  
☐ Soy milk  
☐ Rice milk  
☐ Other

Question 6 appears on the next page

**Over the past 12 months...**

6. How often did you drink **meal replacement, energy, or high-protein beverages** such as Instant Breakfast, Ensure, Slimfast, Sustacal or others?

☐ NEVER (GO TO QUESTION 7)

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2–3 times per month      | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 1–2 times per week       | <input type="checkbox"/> 4–5 times per day       |
| <input type="checkbox"/> 3–4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week       |  |

- 6a. Each time you drank **meal replacement beverages**, how much did you usually drink?

- ☐ Less than 1 cup (8 ounces)  
☐ 1 to 1½ cups (8 to 12 ounces)  
☐ More than 1½ cups (12 ounces)

7. Over the past 12 months, did you drink **soft drinks, soda, or pop**?

☐ NO (GO TO QUESTION 8)

☐ YES

- 7a. How often did you drink **soft drinks, soda, or pop IN THE SUMMER**?

☐ NEVER

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2–3 times per month      | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 1–2 times per week       | <input type="checkbox"/> 4–5 times per day       |
| <input type="checkbox"/> 3–4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week       |  |

- 7b. How often did you drink **soft drinks, soda, or pop DURING THE REST OF THE YEAR**?

☐ NEVER

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2–3 times per month      | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 1–2 times per week       | <input type="checkbox"/> 4–5 times per day       |
| <input type="checkbox"/> 3–4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week       |  |

- 7c. Each time you drank **soft drinks, soda, or pop**, how much did you usually drink?

- ☐ Less than 12 ounces or less than 1 can or bottle  
☐ 12 to 16 ounces or 1 can or bottle  
☐ More than 16 ounces or more than 1 can or bottle

Question 8 appears in the next column

- 7d. How often were these soft drinks, soda, or pop **diet** or **sugar-free**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

- 7e. How often were these soft drinks, soda, or pop **caffeine-free**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

8. Over the past 12 months, did you drink **beer**?

☐ NO (GO TO QUESTION 9)

☐ YES

- 8a. How often did you drink **beer IN THE SUMMER**?

☐ NEVER

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2–3 times per month      | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 1–2 times per week       | <input type="checkbox"/> 4–5 times per day       |
| <input type="checkbox"/> 3–4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week       |  |

- 8b. How often did you drink **beer DURING THE REST OF THE YEAR**?

☐ NEVER

- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2–3 times per month      | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 1–2 times per week       | <input type="checkbox"/> 4–5 times per day       |
| <input type="checkbox"/> 3–4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week       |  |

- 8c. Each time you drank **beer**, how much did you usually drink?

- ☐ Less than a 12-ounce can or bottle  
☐ 1 to 3 12-ounce cans or bottles  
☐ More than 3 12-ounce cans or bottles



Question 9 appears on the next page

Over the **past 12 months...**

9. How often did you drink **wine** or **wine coolers**?

- ☐ NEVER (GO TO QUESTION 10)
- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2-3 times per month      | <input type="checkbox"/> 2-3 times per day       |
| <input type="checkbox"/> 1-2 times per week       | <input type="checkbox"/> 4-5 times per day       |
| <input type="checkbox"/> 3-4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week       |  |

9a. Each time you drank **wine** or **wine coolers**, how much did you usually drink?

- ☐ Less than 5 ounces or less than 1 glass  
☐ 5 to 12 ounces or 1 to 2 glasses  
☐ More than 12 ounces or more than 2 glasses

10. How often did you drink **liquor** or **mixed drinks**?

- ☐ NEVER (GO TO QUESTION 11)
- |   |  |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2-3 times per month      | <input type="checkbox"/> 2-3 times per day       |
| <input type="checkbox"/> 1-2 times per week       | <input type="checkbox"/> 4-5 times per day       |
| <input type="checkbox"/> 3-4 times per week       | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week       |  |

10a. Each time you drank **liquor** or **mixed drinks**, how much did you usually drink?

- ☐ Less than 1 shot of liquor  
☐ 1 to 3 shots of liquor  
☐ More than 3 shots of liquor

11. Over the **past 12 months**, did you eat **oatmeal**, **grits**, or **other cooked cereal**?

☐ NO (GO TO QUESTION 12)

☐ YES

11a. How often did you eat **oatmeal**, **grits**, or **other cooked cereal** **IN THE WINTER**?

- ☐ NEVER
- |  |  |
|--|--|
| <input type="checkbox"/> 1-6 times per winter  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7-11 times per winter | <input type="checkbox"/> 3-4 times per week      |
| <input type="checkbox"/> 1 time per month      | <input type="checkbox"/> 5-6 times per week      |
| <input type="checkbox"/> 2-3 times per month   | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week       | <input type="checkbox"/> 2 or more times per day |

Question 12 appears in the next column

11b. How often did you eat **oatmeal**, **grits**, or **other cooked cereal** **DURING THE REST OF THE YEAR**?

- ☐ NEVER
- |  |  |
|--|--|
| <input type="checkbox"/> 1-6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5-6 times per week      |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

11c. Each time you ate **oatmeal**, **grits**, or **other cooked cereal**, how much did you usually eat?

- ☐ Less than ¼ cup  
☐ ¼ to 1¼ cups  
☐ More than 1¼ cups

12. How often did you eat **cold cereal**?

- ☐ NEVER (GO TO QUESTION 13)
- |  |  |
|--|--|
| <input type="checkbox"/> 1-6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5-6 times per week      |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

12a. Each time you ate **cold cereal**, how much did you usually eat?

- ☐ Less than 1 cup  
☐ 1 to 2½ cups  
☐ More than 2½ cups

12b. How often was the cold cereal you ate **Total**, **Product 19**, or **Right Start**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

12c. How often was the cold cereal you ate **All Bran**, **Fiber One**, **100% Bran**, or **Bran Buds**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Question 13 appears on the next page



**Over the past 12 months...**

12d. How often was the cold cereal you ate **some other bran or fiber cereal** (such as Cheerios, Shredded Wheat, Raisin Bran, Bran Flakes, Grape-Nuts, Granola, Wheaties, or Healthy Choice)?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

12e. How often was the cold cereal you ate any **other type of cold cereal** (such as Corn Flakes, Rice Krispies, Frosted Flakes, Special K, Froot Loops, Cap'n Crunch, or others)?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

12f. Was **milk** added to your cold cereal?

- ☐ NO (GO TO QUESTION 13)  
☐ YES

12g. What kind of **milk** was usually added?

- ☐ Whole milk  
☐ 2% fat milk  
☐ 1% fat milk  
☐ Skim, nonfat, or ½% fat milk  
☐ Soy milk  
☐ Rice milk  
☐ Other

12h. Each time **milk was added to your cold cereal**, how much was usually added?

- ☐ Less than ½ cup  
☐ ½ to 1 cup  
☐ More than 1 cup

13. How often did you eat **applesauce**?

- ☐ NEVER (GO TO QUESTION 14)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

Question 14 appears in the next column

13a. Each time you ate **applesauce**, how much did you usually eat?

- ☐ Less than ¼ cup  
☐ ¼ to 1 cup  
☐ More than 1 cup

14. How often did you eat **apples**?

- ☐ NEVER (GO TO QUESTION 15)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

14a. Each time you ate **apples**, how many did you usually eat?

- ☐ Less than 1 apple  
☐ 1 apple  
☐ More than 1 apple

15. How often did you eat **pears** (fresh, canned, or frozen)?

- ☐ NEVER (GO TO QUESTION 16)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

15a. Each time you ate **pears**, how many did you usually eat?

- ☐ Less than 1 pear  
☐ 1 pear  
☐ More than 1 pear

16. How often did you eat **bananas**?

- ☐ NEVER (GO TO QUESTION 17)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |



Question 17 appears on the next page

Over the past 12 months...

16a. Each time you ate **bananas**, how many did you usually eat?

- ☐ Less than 1 banana
- ☐ 1 banana
- ☐ More than 1 banana

17. How often did you eat **dried fruit**, such as prunes or raisins (not including dried apricots)?

☐ NEVER (GO TO QUESTION 18)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

17a. Each time you ate **dried fruit**, how much did you usually eat (not including dried apricots)?

- ☐ Less than 2 tablespoons
- ☐ 2 to 5 tablespoons
- ☐ More than 5 tablespoons

18. Over the past 12 months, did you eat **peaches, nectarines, or plums**?

☐ NO (GO TO QUESTION 19)

☐ YES

18a. How often did you eat **fresh peaches, nectarines, or plums WHEN IN SEASON**?

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per season  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month      | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month   | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week       | <input type="checkbox"/> 2 or more times per day |

18b. How often did you eat **peaches, nectarines, or plums** (fresh, canned, or frozen) **DURING THE REST OF THE YEAR**?

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

Question 19 appears in the next column

18c. Each time you ate **peaches, nectarines, or plums**, how much did you usually eat?

- ☐ Less than 1 fruit or less than ½ cup
- ☐ 1 to 2 fruits or ½ to ¾ cup
- ☐ More than 2 fruits or more than ¾ cup

19. How often did you eat **grapes**?

☐ NEVER (GO TO QUESTION 20)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

19a. Each time you ate **grapes**, how much did you usually eat?

- ☐ Less than ½ cup or less than 10 grapes
- ☐ ½ to 1 cup or 10 to 30 grapes
- ☐ More than 1 cup or more than 30 grapes

20. Over the past 12 months, did you eat **cantaloupe**?

☐ NO (GO TO QUESTION 21)

☐ YES

20a. How often did you eat **fresh cantaloupe WHEN IN SEASON**?

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per season  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month      | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month   | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week       | <input type="checkbox"/> 2 or more times per day |

20b. How often did you eat **fresh or frozen cantaloupe DURING THE REST OF THE YEAR**?

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

Question 21 appears on the next page

Over the past 12 months...

20c. Each time you ate **cantaloupe**, how much did you usually eat?

- ☐ Less than ¼ melon or less than ½ cup  
☐ ¼ melon or ½ to 1 cup  
☐ More than ¼ melon or more than 1 cup

21. Over the past 12 months, did you eat **melon, other than cantaloupe** (such as watermelon or honeydew)?

☐ NO (GO TO QUESTION 22)

☐ YES

21a. How often did you eat **fresh melon, other than cantaloupe** (such as watermelon or honeydew) **WHEN IN SEASON?**

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per season  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month      | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month   | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week       | <input type="checkbox"/> 2 or more times per day |

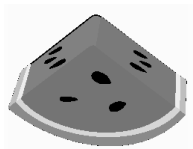
21b. How often did you eat **fresh or frozen melon, other than cantaloupe** (such as watermelon or honeydew) **DURING THE REST OF THE YEAR?**

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

21c. Each time you ate **melon other than cantaloupe**, how much did you usually eat?

- ☐ Less than ½ cup or 1 small wedge  
☐ ½ to 2 cups or 1 medium wedge  
☐ More than 2 cups or 1 large wedge



Question 22 appears in the next column

22. Over the past 12 months, did you eat **strawberries**?

☐ NO (GO TO QUESTION 23)

☐ YES

22a. How often did you eat **fresh strawberries WHEN IN SEASON?**

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per season  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month      | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month   | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week       | <input type="checkbox"/> 2 or more times per day |

22b. How often did you eat **fresh or frozen strawberries DURING THE REST OF THE YEAR?**

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

22c. Each time you ate **strawberries**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 3 berries  
☐ ¼ to ¾ cup or 3 to 8 berries  
☐ More than ¾ cup or more than 8 berries

23. Over the past 12 months, did you eat **oranges, tangerines, or tangelos**?

☐ NO (GO TO QUESTION 24)

☐ YES

23a. How often did you eat **fresh oranges, tangerines, or tangelos WHEN IN SEASON?**

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per season  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month      | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month   | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week       | <input type="checkbox"/> 2 or more times per day |

Question 24 appears on the next page

Over the past 12 months...

23b. How often did you eat **oranges, tangerines, or tangelos** (fresh or canned) **DURING THE REST OF THE YEAR**?

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

23c. Each time you ate **oranges, tangerines, or tangelos**, how many did you usually eat?

- ☐ Less than 1 fruit  
☐ 1 fruit  
☐ More than 1 fruit

24. Over the past 12 months, did you eat **grapefruit**?

☐ NO (GO TO QUESTION 25)

☐ YES

24a. How often did you eat **fresh grapefruit** **WHEN IN SEASON**?

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per season  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month      | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month   | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week       | <input type="checkbox"/> 2 or more times per day |

24b. How often did you eat **grapefruit** (fresh or canned) **DURING THE REST OF THE YEAR**?

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

24c. Each time you ate **grapefruit**, how much did you usually eat?

- ☐ Less than ½ grapefruit  
☐ ½ grapefruit  
☐ More than ½ grapefruit

Question 25 appears in the next column

25. How often did you eat **other kinds of fruit**?

☐ NEVER (GO TO QUESTION 26)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

25a. Each time you ate **other kinds of fruit**, how much did you usually eat?

- ☐ Less than ¼ cup  
☐ ¼ to ¾ cup  
☐ More than ¾ cup

26. How often did you eat **COOKED greens** (such as spinach, turnip, collard, mustard, chard, or kale)?

☐ NEVER (GO TO QUESTION 27)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

26a. Each time you ate **COOKED greens**, how much did you usually eat?

- ☐ Less than ½ cup  
☐ ½ to 1 cup  
☐ More than 1 cup

27. How often did you eat **RAW greens** (such as spinach, turnip, collard, mustard, chard, or kale)?  
*(We will ask about lettuce later.)*

☐ NEVER (GO TO QUESTION 28)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

27a. Each time you ate **RAW greens**, how much did you usually eat?

- ☐ Less than ½ cup  
☐ ½ to 1 cup  
☐ More than 1 cup

Question 28 appears on the next page

Over the **past 12 months...**

28. How often did you eat **coleslaw**?

- ☐ NEVER (GO TO QUESTION 29)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

28a. Each time you ate **coleslaw**, how much did you usually eat?

- ☐ Less than ¼ cup  
☐ ¼ to ¾ cup  
☐ More than ¾ cup

29. How often did you eat **sauerkraut** or **cabbage** (other than coleslaw)?

- ☐ NEVER (GO TO QUESTION 30)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

29a. Each time you ate **sauerkraut** or **cabbage**, how much did you usually eat?

- ☐ Less than ¼ cup  
☐ ¼ to 1 cup  
☐ More than 1 cup

30. How often did you eat **carrots** (fresh, canned, or frozen)?

- ☐ NEVER (GO TO QUESTION 31)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

30a. Each time you ate **carrots**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 2 baby carrots  
☐ ¼ to ½ cup or 2 to 5 baby carrots  
☐ More than ½ cup or more than 5 baby carrots

Question 31 appears in the next column

31. How often did you eat **string beans** or **green beans** (fresh, canned, or frozen)?

- ☐ NEVER (GO TO QUESTION 32)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

31a. Each time you ate **string beans** or **green beans**, how much did you usually eat?

- ☐ Less than ½ cup  
☐ ½ to 1 cup  
☐ More than 1 cup

32. How often did you eat **peas** (fresh, canned, or frozen)?

- ☐ NEVER (GO TO QUESTION 33)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

32a. Each time you ate **peas**, how much did you usually eat?

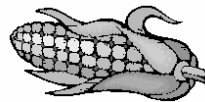
- ☐ Less than ¼ cup  
☐ ¼ to ¾ cup  
☐ More than ¾ cup

33. Over the **past 12 months**, did you eat **corn**?

- ☐ NO (GO TO QUESTION 34)  
☐ YES

33a. How often did you eat **fresh corn WHEN IN SEASON**?

- ☐ NEVER
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per season  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month      | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month   | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week       | <input type="checkbox"/> 2 or more times per day |



Question 34 appears on the next page

Over the past 12 months...

33b. How often did you eat **corn** (fresh, canned, or frozen) **DURING THE REST OF THE YEAR**?

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

33c. Each time you ate **corn**, how much did you usually eat?

- ☐ Less than 1 ear or less than ½ cup  
☐ 1 ear or ½ to 1 cup  
☐ More than 1 ear or more than 1 cup

34. Over the past 12 months, how often did you eat **broccoli** (fresh or frozen)?

☐ NEVER (GO TO QUESTION 35)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

34a. Each time you ate **broccoli**, how much did you usually eat?

- ☐ Less than ¼ cup  
☐ ¼ to 1 cup  
☐ More than 1 cup

35. How often did you eat **cauliflower** or **Brussels sprouts** (fresh or frozen)?

☐ NEVER (GO TO QUESTION 36)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

35a. Each time you ate **cauliflower** or **Brussels sprouts**, how much did you usually eat?

- ☐ Less than ¼ cup  
☐ ¼ to ½ cup  
☐ More than ½ cup

Question 36 appears in the next column

36. How often did you eat mixed **vegetables**?

☐ NEVER (GO TO QUESTION 37)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

36a. Each time you ate **mixed vegetables**, how much did you usually eat?

- ☐ Less than ½ cup  
☐ ½ to 1 cup  
☐ More than 1 cup

37. How often did you eat **onions**?

☐ NEVER (GO TO QUESTION 38)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

37a. Each time you ate **onions**, how much did you usually eat?

- ☐ Less than 1 slice or less than 1 tablespoon  
☐ 1 slice or 1 to 4 tablespoons  
☐ More than 1 slice or more than 4 tablespoons

38. Now think about all the **cooked vegetables** you ate in the past 12 months and how they were prepared. How often were your vegetables **COOKED WITH** some sort of **fat**, including oil spray? (*Please do not include potatoes.*)

☐ NEVER (GO TO QUESTION 39)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |



Question 39 appears on the next page

Over the past 12 months...

38a. Which fats were usually added to your vegetables **DURING COOKING**? (Please do not include potatoes. **Mark all that apply.**)

- |  |   |
|--|---|
| <input type="checkbox"/> Margarine (including low-fat) | <input type="checkbox"/> Corn oil                         |
| <input type="checkbox"/> Butter (including low-fat)    | <input type="checkbox"/> Canola or rapeseed oil           |
| <input type="checkbox"/> Lard, fatback, or bacon fat   | <input type="checkbox"/> Oil spray, such as Pam or others |
| <input type="checkbox"/> Olive oil                     | <input type="checkbox"/> Other kinds of oils              |
|  | <input type="checkbox"/> None of the above                |

39. Now, thinking again about all the **cooked vegetables** you ate in the past 12 months, how often was some sort of fat, sauce, or dressing added **AFTER COOKING OR AT THE TABLE**? (Please do not include potatoes.)

☐ NEVER (GO TO QUESTION 40)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 2 times per day         |
| <input type="checkbox"/> 1–2 times per week  | <input type="checkbox"/> 3 or more times per day |

39a. Which fats, sauces, or dressings were usually added **AFTER COOKING OR AT THE TABLE**? (Please do not include potatoes. **Mark all that apply.**)

- |  |   |
|--|---|
| <input type="checkbox"/> Margarine (including low-fat) | <input type="checkbox"/> Salad dressing |
| <input type="checkbox"/> Butter (including low-fat)    | <input type="checkbox"/> Cheese sauce   |
| <input type="checkbox"/> Lard, fatback, or bacon fat   | <input type="checkbox"/> White sauce    |
|  | <input type="checkbox"/> Other          |

39b. If margarine, butter, lard, fatback, or bacon fat was added to your cooked vegetables **AFTER COOKING OR AT THE TABLE**, how much did you usually add?

- ☐ Did not usually add these
- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

39c. If salad dressing, cheese sauce, or white sauce was added to your cooked vegetables **AFTER COOKING OR AT THE TABLE**, how much did you usually add?

- ☐ Did not usually add these
- ☐ Less than 1 tablespoon
- ☐ 1 to 3 tablespoons
- ☐ More than 3 tablespoons

Question 40 appears in the next column

40. Over the past 12 months, how often did you eat **sweet peppers** (green, red, or yellow)?

☐ NEVER (GO TO QUESTION 41)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

40a. Each time you ate **sweet peppers**, how much did you usually eat?

- ☐ Less than 1/8 pepper
- ☐ 1/8 to 1/4 pepper
- ☐ More than 1/4 pepper

41. Over the past 12 months, did you eat **fresh tomatoes** (including those in salads)?

☐ NO (GO TO QUESTION 42)

☐ YES

41a. How often did you eat **fresh tomatoes** (including those in salads) **WHEN IN SEASON**?

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per season  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month      | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month   | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week       | <input type="checkbox"/> 2 or more times per day |

41b. How often did you eat **fresh tomatoes** (including those in salads) **DURING THE REST OF THE YEAR**?

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

41c. Each time you ate **fresh tomatoes**, how much did you usually eat?

- ☐ Less than 1/4 tomato
- ☐ 1/4 to 1/2 tomato
- ☐ More than 1/2 tomato

Question 42 appears on the next page

Over the **past 12 months...**

42. How often did you eat **lettuce salads** (with or without other vegetables)?

- ☐ NEVER (GO TO QUESTION 43)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

42a. Each time you ate **lettuce salads**, how much did you usually eat?

- ☐ Less than ¼ cup  
☐ ¼ to 1¼ cups  
☐ More than 1¼ cups

43. How often did you eat **salad dressing** (including low-fat) on salads?

- ☐ NEVER (GO TO QUESTION 44)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

43a. Each time you ate **salad dressing** on salads, how much did you usually eat?

- ☐ Less than 2 tablespoons  
☐ 2 to 4 tablespoons  
☐ More than 4 tablespoons

44. How often did you eat **sweet potatoes** or **yams**?

- ☐ NEVER (GO TO QUESTION 45)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

44a. Each time you ate **sweet potatoes** or **yams**, how much did you usually eat?

- ☐ 1 small potato or less than ¼ cup  
☐ 1 medium potato or ¼ to ¾ cup  
☐ 1 large potato or more than ¾ cup

Question 45 appears in the next column

45. How often did you eat **French fries, home fries, hash browned potatoes, or tater tots**?

- ☐ NEVER (GO TO QUESTION 46)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

45a. Each time you ate **French fries, home fries, hash browned potatoes, or tater tots** how much did you usually eat?

- ☐ Less than 10 fries or less than ½ cup  
☐ 10 to 25 fries or ½ to 1 cup  
☐ More than 25 fries or more than 1 cup

46. How often did you eat **potato salad**?

- ☐ NEVER (GO TO QUESTION 47)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

46a. Each time you ate **potato salad**, how much did you usually eat?

- ☐ Less than ½ cup  
☐ ½ to 1 cup  
☐ More than 1 cup

47. How often did you eat **baked, boiled, or mashed potatoes**?

- ☐ NEVER (GO TO QUESTION 48)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

47a. Each time you ate **baked, boiled, or mashed potatoes**, how much did you usually eat?

- ☐ 1 small potato or less than ¼ cup  
☐ 1 medium potato or ½ to 1 cup  
☐ 1 large potato or more than 1 cup

Question 48 appears on the next page



Over the **past 12 months...**

47b. How often was **sour cream** (including low-fat) added to your potatoes, **EITHER IN COOKING OR AT THE TABLE**?

- ☐ Almost never or never (GO TO QUESTION 47d)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

47c. Each time **sour cream** was added to your potatoes, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 3 tablespoons
- ☐ More than 3 tablespoons

→ 47d. How often was **margarine** (including low-fat) added to your potatoes, **EITHER IN COOKING OR AT THE TABLE**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

47e. How often was **butter** (including low-fat) added to your potatoes, **EITHER IN COOKING OR AT THE TABLE**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

47f. Each time **margarine** or **butter** was added to your potatoes, how much was usually added?

- ☐ Never added
- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

47g. How often was **cheese** or **cheese sauce** added to your potatoes, **EITHER IN COOKING OR AT THE TABLE**?

- ☐ Almost never or never (GO TO QUESTION 48)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 48 appears in the next column

47h. Each time **cheese** or **cheese sauce** was added to your potatoes, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 3 tablespoons
- ☐ More than 3 tablespoons

48. How often did you eat **salsa**?

- ☐ NEVER (GO TO QUESTION 49)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

48a. Each time you ate **salsa**, how much did you usually eat?

- ☐ Less than 1 tablespoon
- ☐ 1 to 5 tablespoons
- ☐ More than 5 tablespoons

49. How often did you eat **catsup**?

- ☐ NEVER (GO TO QUESTION 50)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

49a. Each time you ate **catsup**, how much did you usually eat?

- ☐ Less than 1 teaspoon
- ☐ 1 to 6 teaspoons
- ☐ More than 6 teaspoons

50. How often did you eat **stuffing, dressing, or dumplings**?

- ☐ NEVER (GO TO QUESTION 51)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

50a. Each time you ate **stuffing, dressing, or dumplings**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1 cup
- ☐ More than 1 cup

Question 51 appears on the next page

Over the **past 12 months...**

51. How often did you eat **chili**?

- ☐ NEVER (GO TO QUESTION 52)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

51a. Each time you ate **chili**, how much did you usually eat?

- ☐ Less than ½ cup  
☐ ½ to 1¼ cups  
☐ More than 1¼ cups

52. How often did you eat **Mexican foods** (such as tacos, tostados, burritos, tamales, fajitas, enchiladas, quesadillas, and chimichangas)?

- ☐ NEVER (GO TO QUESTION 53)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

52a. Each time you ate **Mexican foods**, how much did you usually eat?

- ☐ Less than 1 taco, burrito, etc.  
☐ 1 to 2 tacos, burritos, etc.  
☐ More than 2 tacos, burritos, etc.

53. How often did you eat **cooked dried beans** (such as baked beans, pintos, kidney, blackeyed peas, lima, lentils, soybeans, or refried beans)? *(Please don't include bean soups or chili.)*

- ☐ NEVER (GO TO QUESTION 54)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

53a. Each time you ate **beans**, how much did you usually eat?

- ☐ Less than ½ cup  
☐ ½ to 1 cup  
☐ More than 1 cup

Question 54 appears in the next column

53b. How often were the beans you ate **refried beans, beans prepared with any type of fat, or with meat added**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

54. How often did you eat **other kinds of vegetables**?

- ☐ NEVER (GO TO QUESTION 55)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

54a. Each time you ate **other kinds of vegetables**, how much did you usually eat?

- ☐ Less than ¼ cup  
☐ ¼ to ½ cup  
☐ More than ½ cup

55. How often did you eat **rice or other cooked grains** (such as bulgur, cracked wheat, or millet)?

- ☐ NEVER (GO TO QUESTION 56)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

55a. Each time you ate **rice or other cooked grains**, how much did you usually eat?

- ☐ Less than ½ cup  
☐ ½ to 1½ cups  
☐ More than 1½ cups

55b. How often was **butter, margarine, or oil** added to your rice **IN COOKING OR AT THE TABLE**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Question 56 appears on the next page

Over the **past 12 months...**

56. How often did you eat **pancakes, waffles, or French toast**?

- ☐ NEVER (GO TO QUESTION 57)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

56a. Each time you ate **pancakes, waffles, or French toast**, how much did you usually eat?

- ☐ Less than 1 medium piece  
☐ 1 to 3 medium pieces  
☐ More than 3 medium pieces

56b. How often was **margarine** (including low-fat) added to your pancakes, waffles, or French toast **AFTER COOKING OR AT THE TABLE**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

56c. How often was **butter** (including low-fat) added to your pancakes, waffles, or French toast **AFTER COOKING OR AT THE TABLE**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

56d. Each time **margarine** or **butter** was added to your pancakes, waffles, or French toast, how much was usually added?

- ☐ Never added  
☐ Less than 1 teaspoon  
☐ 1 to 3 teaspoons  
☐ More than 3 teaspoons

56e. How often was **syrup** added to your pancakes, waffles, or French toast?

- ☐ Almost never or never (GO TO QUESTION 57)  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Question 57 appears in the next column

56f. Each time **syrup** was added to your pancakes, waffles, or French toast, how much was usually added?

- ☐ Less than 1 tablespoon  
☐ 1 to 4 tablespoons  
☐ More than 4 tablespoons

57. How often did you eat **lasagna, stuffed shells, stuffed manicotti, ravioli, or tortellini**? (Please do not include spaghetti or other pasta.)

- ☐ NEVER (GO TO QUESTION 58)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

57a. Each time you ate **lasagna, stuffed shells, stuffed manicotti, ravioli, or tortellini**, how much did you usually eat?

- ☐ Less than 1 cup  
☐ 1 to 2 cups  
☐ More than 2 cups

58. How often did you eat **macaroni and cheese**?

- ☐ NEVER (GO TO QUESTION 59)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

58a. Each time you ate **macaroni and cheese**, how much did you usually eat?

- ☐ Less than 1 cup  
☐ 1 to 1½ cups  
☐ More than 1½ cups

59. How often did you eat **pasta salad** or **macaroni salad**?

- ☐ NEVER (GO TO QUESTION 60)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

Question 60 appears on the next page

Over the **past 12 months...**

59a. Each time you ate **pasta salad** or **macaroni salad**, how much did you usually eat?

- ☐ Less than ½ cup  
☐ ½ to 1 cup  
☐ More than 1 cup

60. Other than the pastas listed in Questions 57, 58, and 59, how often did you eat **pasta, spaghetti, or other noodles**?

☐ NEVER (GO TO QUESTION 61)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

60a. Each time you ate **pasta, spaghetti, or other noodles**, how much did you usually eat?

- ☐ Less than 1 cup  
☐ 1 to 3 cups  
☐ More than 3 cups

60b. How often did you eat your pasta, spaghetti, or other noodles with **tomato sauce** or **spaghetti sauce made WITH meat**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

60c. How often did you eat your pasta, spaghetti, or other noodles with **tomato sauce** or **spaghetti sauce made WITHOUT meat**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

60d. How often did you eat your pasta, spaghetti, or other noodles with **margarine, butter, oil, or cream sauce**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Question 61 appears in the next column

61. How often did you eat **bagels** or **English muffins**?

☐ NEVER (GO TO INTRODUCTION TO QUESTION 62)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

61a. Each time you ate **bagels** or **English muffins**, how many did you usually eat?

- ☐ Less than 1 bagel or English muffin  
☐ 1 bagel or English muffin  
☐ More than 1 bagel or English muffin

61b. How often was **margarine** (including low-fat) added to your bagels or English muffins?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

61c. How often was **butter** (including low-fat) added to your bagels or English muffins?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

61d. Each time **margarine** or **butter** was added to your bagels or English muffins, how much was usually added?

- ☐ Never added  
☐ Less than 1 teaspoon  
☐ 1 to 2 teaspoons  
☐ More than 2 teaspoons

61e. How often was **cream cheese** (including low-fat) spread on your bagels or English muffins?

- ☐ Almost never or never (GO TO INTRODUCTION TO QUESTION 62)  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Introduction to Question 62 appears on the next page

Over the **past 12 months...**

- 61f. Each time **cream cheese** was added to your bagels or English muffins, how much was usually added?

☐ Less than 1 tablespoon  
☐ 1 to 2 tablespoons  
☐ More than 2 tablespoons

The next questions ask about your intake of breads other than bagels or English muffins. First, we will ask about bread you ate as part of sandwiches only. Then we will ask about all other bread you ate.

62. How often did you eat **breads or rolls AS PART OF SANDWICHES** (including burger and hot dog rolls)?

☐ NEVER (GO TO QUESTION 63)

<input type="checkbox"/> 1–6 times per year	<input type="checkbox"/> 2 times per week
<input type="checkbox"/> 7–11 times per year	<input type="checkbox"/> 3–4 times per week
<input type="checkbox"/> 1 time per month	<input type="checkbox"/> 5–6 times per week
<input type="checkbox"/> 2–3 times per month	<input type="checkbox"/> 1 time per day
<input type="checkbox"/> 1 time per week	<input type="checkbox"/> 2 or more times per day

- 62a. Each time you ate **breads or rolls AS PART OF SANDWICHES**, how many did you usually eat?

☐ 1 slice or ½ roll  
☐ 2 slices or 1 roll  
☐ More than 2 slices or more than 1 roll

- 62b. How often were the breads or rolls that you used for your sandwiches **white bread** (including burger and hot dog rolls)?

☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

- 62c. How often was **mayonnaise or mayonnaise-type dressing** (including low-fat) added to your sandwich bread or rolls?

☐ Almost never or never (GO TO QUESTION 62e)  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Question 62e appears in the next column  
 Question 63 appears in the next column

- 62d. Each time **mayonnaise or mayonnaise-type dressing** was added to your sandwich breads or rolls, how much was usually added?

☐ Less than 1 teaspoon  
☐ 1 to 3 teaspoons  
☐ More than 3 teaspoons

- 62e. How often was **margarine** (including low-fat) added to your sandwich bread or rolls?

☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

- 62f. How often was **butter** (including low-fat) added to your sandwich bread or rolls?

☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

- 62g. Each time **margarine or butter** was added to your sandwich breads or rolls, how much was usually added?

☐ Never added  
☐ Less than 1 teaspoon  
☐ 1 to 2 teaspoons  
☐ More than 2 teaspoons

63. How often did you eat **breads or dinner rolls, NOT AS PART OF SANDWICHES**?

☐ NEVER (GO TO QUESTION 64)

<input type="checkbox"/> 1–6 times per year	<input type="checkbox"/> 2 times per week
<input type="checkbox"/> 7–11 times per year	<input type="checkbox"/> 3–4 times per week
<input type="checkbox"/> 1 time per month	<input type="checkbox"/> 5–6 times per week
<input type="checkbox"/> 2–3 times per month	<input type="checkbox"/> 1 time per day
<input type="checkbox"/> 1 time per week	<input type="checkbox"/> 2 or more times per day

- 63a. Each time you ate **breads or dinner rolls, NOT AS PART OF SANDWICHES**, how much did you usually eat?

☐ 1 slice or 1 dinner roll  
☐ 2 slices or 2 dinner rolls  
☐ More than 2 slices or 2 dinner rolls



Question 64 appears on the next page

Over the **past 12 months...**

63b. How often were the breads or rolls you ate **white bread**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

63c. How often was **margarine** (including low-fat) added to your breads or rolls?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

63d. How often was **butter** (including low-fat) added to your breads or rolls?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

63e. Each time **margarine** or **butter** was added to your breads or rolls, how much was usually added?

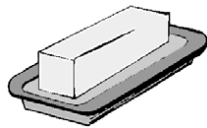
- ☐ Never added
- ☐ Less than 1 teaspoon
- ☐ 1 to 2 teaspoons
- ☐ More than 2 teaspoons

63f. How often was **cream cheese** (including low-fat) added to your breads or rolls?

- ☐ Almost never or never (GO TO QUESTION 64)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

63g. Each time **cream cheese** was added to your breads or rolls, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 2 tablespoons
- ☐ More than 2 tablespoons



Question 64 appears in the next column

64. How often did you eat **jam, jelly, or honey** on bagels, muffins, bread, rolls, or crackers?

- ☐ NEVER (GO TO QUESTION 65)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

64a. Each time you ate **jam, jelly, or honey**, how much did you usually eat?

- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

65. How often did you eat **peanut butter or other nut butter**?

- ☐ NEVER (GO TO QUESTION 66)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

65a. Each time you ate **peanut butter or other nut butter**, how much did you usually eat?

- ☐ Less than 1 tablespoon
- ☐ 1 to 2 tablespoons
- ☐ More than 2 tablespoons

66. How often did you eat **roast beef or steak IN SANDWICHES**?

- ☐ NEVER (GO TO QUESTION 67)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

66a. Each time you ate **roast beef or steak IN SANDWICHES**, how much did you usually eat?

- ☐ Less than 1 slice or less than 2 ounces
- ☐ 1 to 2 slices or 2 to 4 ounces
- ☐ More than 2 slices or more than 4 ounces

Question 67 appears on the next page

Over the **past 12 months...**

67. How often did you eat **turkey or chicken COLD CUTS** (such as loaf, luncheon meat, turkey ham, turkey salami, or turkey pastrami)? *(We will ask about other turkey or chicken later.)*

☐ NEVER (GO TO QUESTION 68)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

67a. Each time you ate **turkey or chicken COLD CUTS**, how much did you usually eat?

- ☐ Less than 1 slice  
☐ 1 to 3 slices  
☐ More than 3 slices

68. How often did you eat **luncheon or deli-style ham**? *(We will ask about other ham later.)*

☐ NEVER (GO TO QUESTION 69)

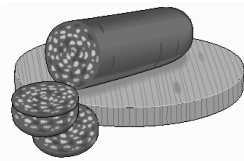
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

68a. Each time you ate **luncheon or deli-style ham**, how much did you usually eat?

- ☐ Less than 1 slice  
☐ 1 to 3 slices  
☐ More than 3 slices

68b. How often was the luncheon or deli-style ham you ate **light, low-fat, or fat-free**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always



Question 69 appears in the next column

69. How often did you eat **other cold cuts or luncheon meats** (such as bologna, salami, corned beef, pastrami, or others, including low-fat)? *(Please do not include ham, turkey, or chicken cold cuts.)*

☐ NEVER (GO TO QUESTION 70)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

69a. Each time you ate **other cold cuts or luncheon meats**, how much did you usually eat?

- ☐ Less than 1 slice  
☐ 1 to 3 slices  
☐ More than 3 slices

69b. How often were the other cold cuts or luncheon meats you ate **light, low-fat, or fat-free cold cuts or luncheon meats**? *(Please do not include ham, turkey, or chicken cold cuts.)*

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

70. How often did you eat **canned tuna** (including in salads, sandwiches, or casseroles)?

☐ NEVER (GO TO QUESTION 71)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

70a. Each time you ate **canned tuna**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 2 ounces  
☐ ¼ to ½ cup or 2 to 3 ounces  
☐ More than ½ cup or more than 3 ounces

70b. How often was the canned tuna you ate **water-packed tuna**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Question 71 appears on the next page

Over the **past 12 months...**

70c. How often was the canned tuna you ate **prepared with mayonnaise or other dressing** (including low-fat)?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

71. How often did you eat **GROUND chicken or turkey?** (*We will ask about other chicken and turkey later.*)

☐ NEVER (GO TO QUESTION 72)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

71a. Each time you ate **GROUND chicken or turkey**, how much did you usually eat?

- ☐ Less than 2 ounces or less than ½ cup
- ☐ 2 to 4 ounces or ½ to 1 cup
- ☐ More than 4 ounces or more than 1 cup

72. How often did you eat **beef hamburgers or cheeseburgers?**

☐ NEVER (GO TO QUESTION 73)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

72a. Each time you ate **beef hamburgers or cheeseburgers**, how much did you usually eat?

- ☐ Less than 1 patty or less than 2 ounces
- ☐ 1 patty or 2 to 4 ounces
- ☐ More than 1 patty or more than 4 ounces

72b. How often were the beef hamburgers or cheeseburgers you ate made with **lean ground beef?**

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 73 appears in the next column

73. How often did you eat **ground beef in mixtures** (such as meatballs, casseroles, chili, or meatloaf)?

☐ NEVER (GO TO QUESTION 74)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

73a. Each time you ate **ground beef in mixtures**, how much did you usually eat?

- ☐ Less than 3 ounces or less than ½ cup
- ☐ 3 to 8 ounces or ½ to 1 cup
- ☐ More than 8 ounces or more than 1 cup

74. How often did you eat **hot dogs or frankfurters?** (*Please do not include sausages or vegetarian hot dogs.*)

☐ NEVER (GO TO QUESTION 75)

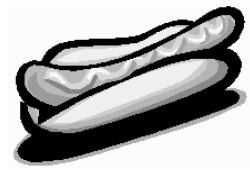
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

74a. Each time you ate **hot dogs or frankfurters**, how many did you usually eat?

- ☐ Less than 1 hot dog
- ☐ 1 to 2 hot dogs
- ☐ More than 2 hot dogs

74b. How often were the hot dogs or frankfurters you ate **light or low-fat hot dogs?**

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always



Question 75 appears on the next page



Over the **past 12 months...**

75. How often did you eat beef mixtures such as **beef stew, beef pot pie, beef and noodles, or beef and vegetables?**

☐ NEVER (GO TO QUESTION 76)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

75a. Each time you ate **beef stew, beef pot pie, beef and noodles, or beef and vegetables**, how much did you usually eat?

- ☐ Less than 1 cup  
☐ 1 to 2 cups  
☐ More than 2 cups

76. How often did you eat **roast beef or pot roast?** *(Please do not include roast beef or pot roast in sandwiches.)*

☐ NEVER (GO TO QUESTION 77)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

76a. Each time you ate **roast beef or pot roast** (including in mixtures), how much did you usually eat?

- ☐ Less than 2 ounces  
☐ 2 to 5 ounces  
☐ More than 5 ounces

77. How often did you eat **steak** (beef)? *(Do not include steak in sandwiches)*

☐ NEVER (GO TO QUESTION 78)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

77a. Each time you ate **steak** (beef), how much did you usually eat?

- ☐ Less than 3 ounces  
☐ 3 to 7 ounces  
☐ More than 7 ounces

Question 78 appears in the next column

77b. How often was the steak you ate **lean steak**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

78. How often did you eat **pork or beef spareribs**?

☐ NEVER (GO TO QUESTION 79)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

78a. Each time you ate **pork or beef spareribs**, how much did you usually eat?

- ☐ Less than 4 ribs  
☐ 4 to 12 ribs  
☐ More than 12 ribs

79. How often did you eat **roast turkey, turkey cutlets, or turkey nuggets** (including in sandwiches)?

☐ NEVER (GO TO QUESTION 80)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

79a. Each time you ate **roast turkey, turkey cutlets, or turkey nuggets**, how much did you usually eat? *(Please note: 4 to 8 turkey nuggets = 3 ounces.)*

- ☐ Less than 2 ounces  
☐ 2 to 4 ounces  
☐ More than 4 ounces

80. How often did you eat **chicken** as part of **salads, sandwiches, casseroles, stews, or other mixtures**?

☐ NEVER (GO TO QUESTION 81)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

Question 81 appears on the next page

Over the **past 12 months...**

80a. Each time you ate **chicken** as part of **salads, sandwiches, casseroles, stews, or other mixtures**, how much did you usually eat?

- ☐ Less than ½ cup  
☐ ½ to 1½ cups  
☐ More than 1½ cups

81. How often did you eat **baked, broiled, roasted, stewed, or fried chicken** (including nuggets)?  
*(Please do not include chicken in mixtures.)*

- ☐ NEVER (GO TO QUESTION 82)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

81a. Each time you ate **baked, broiled, roasted, stewed, or fried chicken** (including nuggets), how much did you usually eat?

- ☐ Less than 2 drumsticks or wings, less than 1 breast or thigh, or less than 4 nuggets  
☐ 2 drumsticks or wings, 1 breast or thigh, or 4 to 8 nuggets  
☐ More than 2 drumsticks or wings, more than 1 breast or thigh, or more than 8 nuggets

81b. How often was the chicken you ate **fried chicken** (including deep fried) or **chicken nuggets**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

81c. How often was the chicken you ate **WHITE meat**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

81d. How often did you eat chicken **WITH skin**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Question 82 appears in the next column

82. How often did you eat **baked ham or ham steak**?

- ☐ NEVER (GO TO QUESTION 83)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

82a. Each time you ate **baked ham or ham steak**, how much did you usually eat?

- ☐ Less than 1 ounce  
☐ 1 to 3 ounces  
☐ More than 3 ounces

83. How often did you eat **pork** (including chops, roasts, and in mixed dishes)? *(Please do not include ham, ham steak, or sausage.)*

- ☐ NEVER (GO TO QUESTION 84)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

83a. Each time you ate **pork**, how much did you usually eat?

- ☐ Less than 2 ounces or less than 1 chop  
☐ 2 to 5 ounces or 1 chop  
☐ More than 5 ounces or more than 1 chop

84. How often did you eat **gravy** on meat, chicken, potatoes, rice, etc.?

- ☐ NEVER (GO TO QUESTION 85)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

84a. Each time you ate **gravy** on meat, chicken, potatoes, rice, etc., how much did you usually eat?

- ☐ Less than ¼ cup  
☐ ¼ to ½ cup  
☐ More than ½ cup

Question 85 appears on the next page

**Over the past 12 months...**

85. How often did you eat **liver** (all kinds) or **liverwurst**?

- ☐ NEVER (GO TO QUESTION 86)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

85a. Each time you ate **liver** or **liverwurst**, how much did you usually eat?

- ☐ Less than 1 ounce  
☐ 1 to 4 ounces  
☐ More than 4 ounces

86. How often did you eat **bacon** (including low-fat)?

- ☐ NEVER (GO TO QUESTION 87)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

86a. Each time you ate **bacon**, how much did you usually eat?

- ☐ Fewer than 2 slices  
☐ 2 to 3 slices  
☐ More than 3 slices

86b. How often was the bacon you ate **light, low-fat, or lean bacon**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

87. How often did you eat **sausage** (including low-fat)?

- ☐ NEVER (GO TO QUESTION 88)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

Question 88 appears in the next column

87a. Each time you ate **sausage**, how much did you usually eat?

- ☐ Less than 1 patty or 2 links  
☐ 1 to 3 patties or 2 to 5 links  
☐ More than 3 patties or 5 links

87b. How often was the sausage you ate **light, low-fat, or lean sausage**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

88. How often did you eat **fish sticks** or **fried fish** (including fried seafood or shellfish)?

- ☐ NEVER (GO TO QUESTION 89)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

88a. Each time you ate **fish sticks** or **fried fish**, how much did you usually eat?

- ☐ Less than 2 ounces or less than 1 fillet  
☐ 2 to 7 ounces or 1 fillet  
☐ More than 7 ounces or more than 1 fillet

89. How often did you eat **fish** or **seafood that was NOT FRIED** (including shellfish)?

- ☐ NEVER (GO TO INTRODUCTION TO QUESTION 90)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

89a. Each time you ate eat **fish** or **seafood that was NOT FRIED**, how much did you usually eat?

- ☐ Less than 2 ounces or less than 1 fillet  
☐ 2 to 5 ounces or 1 fillet  
☐ More than 5 ounces or more than 1 fillet



Introduction to Question 90 appears on the next page

Over the past 12 months...

Now think about all the meat, poultry, and fish you ate in the past 12 months and how they were prepared.

90. How often was **oil, butter, margarine, or other fat** used to **FRY, SAUTE, BASTE, OR MARINATE** any meat, poultry, or fish you ate?  
(Please do not include deep frying.)

☐ NEVER (GO TO QUESTION 91)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

90a. Which of the following **fats** were regularly used to prepare your meat, poultry, or fish?  
(Mark all that apply.)

- |  |   |
|--|---|
| <input type="checkbox"/> Margarine (including low-fat) | <input type="checkbox"/> Corn oil                         |
| <input type="checkbox"/> Butter (including low-fat)    | <input type="checkbox"/> Canola or rapeseed oil           |
| <input type="checkbox"/> Lard, fatback, or bacon fat   | <input type="checkbox"/> Oil spray, such as Pam or others |
| <input type="checkbox"/> Olive oil                     | <input type="checkbox"/> Other kinds of oils              |
|  | <input type="checkbox"/> None of the above                |

91. How often did you eat **tofu, soy burgers, or soy meat-substitutes**?

☐ NEVER (GO TO QUESTION 92)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

91a. Each time you ate **tofu, soy burgers, or soy meat-substitutes**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 2 ounces  
☐ ¼ to ½ cup or 2 to 4 ounces  
☐ More than ½ cup or more than 4 ounces

Question 92 appears in the next column

92. Over the past 12 months, did you eat **soups**?

☐ NO (GO TO QUESTION 93)

☐ YES

92a. How often did you eat **soup DURING THE WINTER**?

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per winter  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per winter | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month      | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month   | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week       | <input type="checkbox"/> 2 or more times per day |

92b. How often did you eat **soup DURING THE REST OF THE YEAR**?

☐ NEVER

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

92c. Each time you ate **soup**, how much did you usually eat?

- ☐ Less than 1 cup  
☐ 1 to 2 cups  
☐ More than 2 cups

92d. How often were the soups you ate **bean soups**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

92e. How often were the soups you ate **cream soups** (including chowders)?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Question 93 appears on the next page

Over the **past 12 months...**

92f. How often were the soups you ate **tomato** or **vegetable soups**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

92g. How often were the soups you ate **broth soups** (including chicken) **with** or **without noodles** or **rice**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

93. How often did you eat **pizza**?

☐ NEVER (GO TO QUESTION 94)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

93a. Each time you ate **pizza**, how much did you usually eat?

- ☐ Less than 1 slice or less than 1 mini pizza
- ☐ 1 to 3 slices or 1 mini pizza
- ☐ More than 3 slices or more than 1 mini pizza

93b. How often did you eat pizza with **pepperoni**, **sausage**, or **other meat**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

94. How often did you eat **crackers**?

☐ NEVER (GO TO QUESTION 95)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

Question 95 appears in the next column

94a. Each time you ate **crackers**, how many did you usually eat?

- ☐ Fewer than 4 crackers
- ☐ 4 to 10 crackers
- ☐ More than 10 crackers

95. How often did you eat **corn bread** or **corn muffins**?

☐ NEVER (GO TO QUESTION 96)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

95a. Each time you ate **corn bread** or **corn muffins**, how much did you usually eat?

- ☐ Less than 1 piece or muffin
- ☐ 1 to 2 pieces or muffins
- ☐ More than 2 pieces or muffins

96. How often did you eat **biscuits**?

☐ NEVER (GO TO QUESTION 97)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

96a. Each time you ate **biscuits**, how many did you usually eat?

- ☐ Fewer than 1 biscuit
- ☐ 1 to 2 biscuits
- ☐ More than 2 biscuits

97. How often did you eat **potato chips**, **tortilla chips**, or **corn chips** (including low-fat, fat-free, or low-salt)?

☐ NEVER (GO TO QUESTION 98)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

Question 98 appears on the next page

**Over the past 12 months...**

97a. Each time you ate **potato chips, tortilla chips, or corn chips**, how much did you usually eat?

- ☐ Fewer than 10 chips or less than 1 cup  
☐ 10 to 25 chips or 1 to 2 cups  
☐ More than 25 chips or more than 2 cups

97b. How often were the chips you ate **Wow chips** or other **chips made with fat substitute** (Olean or Olestra)?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

97c. How often were the chips you ate other **low-fat** or **fat-free chips**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

98. How often did you eat **popcorn** (including low-fat)?

☐ NEVER (GO TO QUESTION 99)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

98a. Each time you ate **popcorn**, how much did you usually eat?

- ☐ Less than 2 cups, popped  
☐ 2 to 5 cups, popped  
☐ More than 5 cups, popped

99. How often did you eat **pretzels**?

☐ NEVER (GO TO QUESTION 100)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

Question 100 appears in the next column

99a. Each time you ate **pretzels**, how many did you usually eat?

- ☐ Fewer than 5 average twists  
☐ 5 to 20 average twists  
☐ More than 20 average twists

100. How often did you eat **peanuts, walnuts, seeds, or other nuts**?

☐ NEVER (GO TO QUESTION 101)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

100a. Each time you ate **peanuts, walnuts, seeds, or other nuts**, how much did you usually eat?

- ☐ Less than ¼ cup  
☐ ¼ to ½ cup  
☐ More than ½ cup

101. How often did you eat **energy, high-protein, or breakfast bars** such as **Power Bars, Balance, Clif, or others**?

☐ NEVER (GO TO QUESTION 102)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

101a. Each time you ate **energy, high-protein, or breakfast bars**, how much did you usually eat?

- ☐ Less than 1 bar  
☐ 1 bar  
☐ More than 1 bar

102. How often did you eat **yogurt** (NOT including frozen yogurt)?

☐ NEVER (GO TO QUESTION 103)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

Question 103 appears on the next page

**Over the past 12 months...**

102a. Each time you ate **yogurt**, how much did you usually eat?

- ☐ Less than ½ cup or less than 1 container
- ☐ ½ to 1 cup or 1 container
- ☐ More than 1 cup or more than 1 container

103. How often did you eat **cottage cheese** (including low-fat)?

☐ NEVER (GO TO QUESTION 104)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

103a. Each time you ate **cottage cheese**, how much did you usually eat?

- ☐ Less than ¼ cup
- ☐ ¼ to 1 cup
- ☐ More than 1 cup

104. How often did you eat **cheese** (including low-fat; including on cheeseburgers or in sandwiches or subs)?

☐ NEVER (GO TO QUESTION 105)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

104a. Each time you ate **cheese**, how much did you usually eat?

- ☐ Less than ½ ounce or less than 1 slice
- ☐ ½ to 1½ ounces or 1 slice
- ☐ More than 1½ ounces or more than 1 slice

104b. How often was the cheese you ate **light** or **low-fat cheese**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 105 appears in the next column

104c. How often was the cheese you ate **fat-free cheese**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

105. How often did you eat **frozen yogurt, sorbet, or ices** (including low-fat or fat-free)?

☐ NEVER (GO TO QUESTION 106)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

105a. Each time you ate **frozen yogurt, sorbet, or ices**, how much did you usually eat?

- ☐ Less than ½ cup or less than 1 scoop
- ☐ ½ to 1 cup or 1 to 2 scoops
- ☐ More than 1 cup or more than 2 scoops

106. How often did you eat **ice cream, ice cream bars, or sherbet** (including low-fat or fat-free)?

☐ NEVER (GO TO QUESTION 107)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

106a. Each time you ate **ice cream, ice cream bars, or sherbet**, how much did you usually eat?

- ☐ Less than ½ cup or less than 1 scoop
- ☐ ½ to 1½ cups or 1 to 2 scoops
- ☐ More than 1½ cups or more than 2 scoops

106b. How often was the ice cream you ate **light, low-fat, or fat-free ice cream** or **sherbet**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 107 appears on the next page

**Over the past 12 months...**

107. How often did you eat **cake** (including low-fat or fat-free)?

- ☐ NEVER (GO TO QUESTION 108)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

107a. Each time you ate **cake**, how much did you usually eat?

- ☐ Less than 1 medium piece  
☐ 1 medium piece  
☐ More than 1 medium piece

107b. How often was the cake you ate **light, low-fat, or fat-free cake**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

108. How often did you eat **cookies or brownies** (including low-fat or fat-free)?

- ☐ NEVER (GO TO QUESTION 109)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

108a. Each time you ate **cookies or brownies**, how much did you usually eat?

- ☐ Less than 2 cookies or 1 small brownie  
☐ 2 to 4 cookies or 1 medium brownie  
☐ More than 4 cookies or 1 large brownie

108b. How often were the cookies or brownies you ate **light, low-fat, or fat-free cookies or brownies**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Question 109 appears in the next column

109. How often did you eat **doughnuts, sweet rolls, Danish, or pop-tarts**?

- ☐ NEVER (GO TO QUESTION 110)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

109a. Each time you ate **doughnuts, sweet rolls, Danish, or pop-tarts**, how much did you usually eat?

- ☐ Less than 1 piece  
☐ 1 to 2 pieces  
☐ More than 2 pieces

110. How often did you eat **sweet muffins or dessert breads** (including low-fat or fat-free)?

- ☐ NEVER (GO TO QUESTION 111)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

110a. Each time you ate **sweet muffins or dessert breads**, how much did you usually eat?

- ☐ Less than 1 medium piece  
☐ 1 medium piece  
☐ More than 1 medium piece

110b. How often were the sweet muffins or dessert breads you ate **light, low-fat, or fat-free sweet muffins or dessert breads**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

111. How often did you eat **fruit crisp, cobbler, or strudel**?

- ☐ NEVER (GO TO QUESTION 112)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

Question 112 appears on the next page



Over the **past 12 months...**

111a. Each time you ate **fruit crisp, cobbler, or strudel**, how much did you usually eat?

- ☐ Less than ½ cup  
☐ ½ to 1 cup  
☐ More than 1 cup

112. How often did you eat **pie**?

☐ NEVER (GO TO QUESTION 113)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

112a. Each time you ate **pie**, how much did you usually eat?

- ☐ Less than ¼ of a pie  
☐ About ¼ of a pie  
☐ More than ¼ of a pie

**The next four questions ask about the kinds of pie you ate. Please read all four questions before answering.**

112b. How often were the pies you ate **fruit pie** (such as apple, blueberry, others)?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

112c. How often were the pies you ate **cream, pudding, custard, or meringue pie**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

112d. How often were the pies you ate **pumpkin or sweet potato pie**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Question 113 appears in the next column

112e. How often were the pies you ate **pecan pie**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

113. How often did you eat **chocolate candy**?

☐ NEVER (GO TO QUESTION 114)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

113a. Each time you ate **chocolate candy**, how much did you usually eat?

- ☐ Less than 1 average bar or less than 1 ounce  
☐ 1 average bar or 1 to 2 ounces  
☐ More than 1 average bar or more than 2 ounces

114. How often did you eat **other candy**?

☐ NEVER (GO TO QUESTION 115)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

114a. Each time you ate **other candy**, how much did you usually eat?

- ☐ Fewer than 2 pieces  
☐ 2 to 9 pieces  
☐ More than 9 pieces

115. How often did you eat **eggs, egg whites, or egg substitutes** (NOT counting eggs in baked goods and desserts)? *(Please include eggs in salads, quiche, and soufflés.)*

☐ NEVER (GO TO QUESTION 116)

- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

Question 116 appears on the next page

**Over the past 12 months...**

115a. Each time you ate **eggs**, how many did you usually eat?

- ☐ 1 egg
- ☐ 2 eggs
- ☐ 3 or more eggs

115b. How often were the eggs you ate **egg substitutes**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

115c. How often were the eggs you ate **egg whites only**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

115d. How often were the eggs you ate **regular whole eggs**?

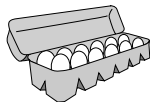
- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

115e. How often were the eggs you ate **cooked in oil, butter, or margarine**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

115f. How often were the eggs you ate part of **egg salad**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always



Question 116 appears in the next column

116. How many cups of **coffee**, caffeinated or decaffeinated, did you drink?

☐ NEVER (GO TO QUESTION 117)

- |  |   |
|--|---|
| <input type="checkbox"/> Less than 1 cup per month | <input type="checkbox"/> 5–6 cups per week      |
| <input type="checkbox"/> 1–3 cups per month        | <input type="checkbox"/> 1 cup per day          |
| <input type="checkbox"/> 1 cup per week            | <input type="checkbox"/> 2–3 cups per day       |
| <input type="checkbox"/> 2–4 cups per week         | <input type="checkbox"/> 4–5 cups per day       |
|  | <input type="checkbox"/> 6 or more cups per day |

116a. How often was the coffee you drank **decaffeinated**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

117. How many glasses of **ICED tea**, caffeinated or decaffeinated, did you drink?

☐ NEVER (GO TO QUESTION 118)

- |  |   |
|--|---|
| <input type="checkbox"/> Less than 1 cup per month | <input type="checkbox"/> 5–6 cups per week      |
| <input type="checkbox"/> 1–3 cups per month        | <input type="checkbox"/> 1 cup per day          |
| <input type="checkbox"/> 1 cup per week            | <input type="checkbox"/> 2–3 cups per day       |
| <input type="checkbox"/> 2–4 cups per week         | <input type="checkbox"/> 4–5 cups per day       |
|  | <input type="checkbox"/> 6 or more cups per day |

117a. How often was the iced tea you drank **decaffeinated or herbal tea**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

118. How many cups of **HOT tea**, caffeinated or decaffeinated, did you drink?

☐ NEVER (GO TO QUESTION 119)

- |  |   |
|--|---|
| <input type="checkbox"/> Less than 1 cup per month | <input type="checkbox"/> 5–6 cups per week      |
| <input type="checkbox"/> 1–3 cups per month        | <input type="checkbox"/> 1 cup per day          |
| <input type="checkbox"/> 1 cup per week            | <input type="checkbox"/> 2–3 cups per day       |
| <input type="checkbox"/> 2–4 cups per week         | <input type="checkbox"/> 4–5 cups per day       |
|  | <input type="checkbox"/> 6 or more cups per day |

118a. How often was the hot tea you drank **decaffeinated or herbal tea**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 119 appears on the next page

Over the **past 12 months...**

119. How often did you add **sugar** or **honey** to your coffee or tea?

- ☐ NEVER (GO TO QUESTION 120)
- |   |  |
|---|--|
| <input type="checkbox"/> Less than 1 time per month | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 1–3 times per month        | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week            | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 2–4 times per week         | <input type="checkbox"/> 4–5 times per day       |
|   | <input type="checkbox"/> 6 or more times per day |

119a. Each time **sugar** or **honey** was added to your coffee or tea, how much was usually added?

- ☐ Less than 1 teaspoon  
☐ 1 to 3 teaspoons  
☐ More than 3 teaspoons

120. How often did you add **artificial sweetener** to your coffee or tea?

- ☐ NEVER (GO TO QUESTION 121)
- |   |  |
|---|--|
| <input type="checkbox"/> Less than 1 time per month | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 1–3 times per month        | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week            | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 2–4 times per week         | <input type="checkbox"/> 4–5 times per day       |
|   | <input type="checkbox"/> 6 or more times per day |

120a. What kind of **artificial sweetener** did you usually use?

- ☐ Equal or aspartame  
☐ Sweet N Low or saccharin

121. How often was **non-dairy creamer** added to your coffee or tea?

- ☐ NEVER (GO TO QUESTION 122)
- |   |  |
|---|--|
| <input type="checkbox"/> Less than 1 time per month | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 1–3 times per month        | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week            | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 2–4 times per week         | <input type="checkbox"/> 4–5 times per day       |
|   | <input type="checkbox"/> 6 or more times per day |

121a. Each time **non-dairy creamer** was added to your coffee or tea, how much was usually used?

- ☐ Less than 1 teaspoon  
☐ 1 to 3 teaspoons  
☐ More than 3 teaspoons

Question 122 appears in the next column

121b. What kind of **non-dairy creamer** did you usually use?

- ☐ Regular powdered  
☐ Low-fat or fat-free powdered  
☐ Regular liquid  
☐ Low-fat or fat-free liquid

122. How often was **cream** or **half and half** added to your coffee or tea?

- ☐ NEVER (GO TO QUESTION 123)
- |   |  |
|---|--|
| <input type="checkbox"/> Less than 1 time per month | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 1–3 times per month        | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week            | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 2–4 times per week         | <input type="checkbox"/> 4–5 times per day       |
|   | <input type="checkbox"/> 6 or more times per day |

122a. Each time **cream** or **half and half** was added to your coffee or tea, how much was usually added?

- ☐ Less than 1 tablespoon  
☐ 1 to 2 tablespoons  
☐ More than 2 tablespoons

123. How often was **milk** added to your coffee or tea?

- ☐ NEVER (GO TO QUESTION 124)
- |   |  |
|---|--|
| <input type="checkbox"/> Less than 1 time per month | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 1–3 times per month        | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week            | <input type="checkbox"/> 2–3 times per day       |
| <input type="checkbox"/> 2–4 times per week         | <input type="checkbox"/> 4–5 times per day       |
|   | <input type="checkbox"/> 6 or more times per day |

123a. Each time **milk** was added to your coffee or tea, how much was usually added?

- ☐ Less than 1 tablespoon  
☐ 1 to 3 tablespoons  
☐ More than 3 tablespoons

123b. What kind of **milk** was usually added to your coffee or tea?

- ☐ Whole milk  
☐ 2% milk  
☐ 1% milk  
☐ Skim, nonfat, or ½% milk  
☐ Evaporated or condensed (canned) milk  
☐ Soy milk  
☐ Rice milk  
☐ Other

Question 124 appears on the next page

Over the **past 12 months...**

124. How often was **sugar** or **honey** added to foods you ate? (Please do not include sugar in coffee, tea, other beverages, or baked goods.)

- ☐ NEVER (GO TO INTRODUCTION TO QUESTION 125)
- |  |  |
|--|--|
| <input type="checkbox"/> 1–6 times per year  | <input type="checkbox"/> 2 times per week        |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week      |
| <input type="checkbox"/> 1 time per month    | <input type="checkbox"/> 5–6 times per week      |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day          |
| <input type="checkbox"/> 1 time per week     | <input type="checkbox"/> 2 or more times per day |

124a. Each time **sugar** or **honey** was added to foods you ate, how much was usually added?

- ☐ Less than 1 teaspoon  
☐ 1 to 3 teaspoons  
☐ More than 3 teaspoons

The following questions are about the kinds of margarine, mayonnaise, sour cream, cream cheese, and salad dressing that you eat. If possible, please check the labels of these foods to help you answer.

125. Over the **past 12 months**, did you eat **margarine**?

- ☐ NO (GO TO QUESTION 126)  
☐ YES

125a. How often was the margarine you ate **regular-fat margarine** (stick or tub)?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

125b. How often was the margarine you ate **light** or **low-fat margarine** (stick or tub)?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Question 126 appears in the next column

125c. How often was the margarine you ate **fat-free margarine**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

126. Over the past 12 months, did you eat **butter**?

- ☐ NO (GO TO QUESTION 127)  
☐ YES

126a. How often was the butter you ate **light** or **low-fat butter**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

127. Over the **past 12 months**, did you eat **mayonnaise** or **mayonnaise-type dressing**?

- ☐ NO (GO TO QUESTION 128)  
☐ YES

127a. How often was the mayonnaise you ate **regular-fat mayonnaise**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

127b. How often was the mayonnaise you ate **light** or **low-fat mayonnaise**?

- ☐ Almost never or never  
☐ About ¼ of the time  
☐ About ½ of the time  
☐ About ¾ of the time  
☐ Almost always or always

Question 128 appears on the next page

Over the past 12 months...

127c. How often was the mayonnaise you ate **fat-free mayonnaise**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

128. Over the past 12 months, did you eat **sour cream**?

☐ NO (GO TO QUESTION 129)

☐ YES

128a. How often was the sour cream you ate **regular-fat sour cream**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

128b. How often was the sour cream you ate **light, low-fat, or fat-free sour cream**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

129. Over the past 12 months, did you eat **cream cheese**?

☐ NO (GO TO QUESTION 130)

☐ YES

129a. How often was the cream cheese you ate **regular-fat cream cheese**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

129b. How often was the cream cheese you ate **light, low-fat, or fat-free cream cheese**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

130. Over the past 12 months, did you eat **salad dressing**?

☐ NO (GO TO INTRODUCTION TO QUESTION 131)

☐ YES

130a. How often was the salad dressing you ate **regular-fat salad dressing** (including oil and vinegar dressing)?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

130b. How often was the salad dressing you ate **light or low-fat salad dressing**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

130c. How often was the salad dressing you ate **fat-free salad dressing**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

**The following two questions ask you to summarize your usual intake of vegetables and fruits. Please do not include salads, potatoes, or juices.**

131. Over the past 12 months, how many servings of **vegetables** (not including salad or potatoes) did you eat per week or per day?

- |   |  |
|---|--|
| <input type="checkbox"/> Less than 1 per week | <input type="checkbox"/> 2 per day         |
| <input type="checkbox"/> 1–2 per week         | <input type="checkbox"/> 3 per day         |
| <input type="checkbox"/> 3–4 per week         | <input type="checkbox"/> 4 per day         |
| <input type="checkbox"/> 5–6 per week         | <input type="checkbox"/> 5 or more per day |
| <input type="checkbox"/> 1 per day            |  |

Question 130 appears in the next column

**Over the past 12 months...**

132. Over the past 12 months, how many servings of **fruit** (not including juices) did you eat per week or per day?

- |   |  |
|---|--|
| <input type="checkbox"/> Less than 1 per week | <input type="checkbox"/> 2 per day         |
| <input type="checkbox"/> 1-2 per week         | <input type="checkbox"/> 3 per day         |
| <input type="checkbox"/> 3-4 per week         | <input type="checkbox"/> 4 per day         |
| <input type="checkbox"/> 5-6 per week         | <input type="checkbox"/> 5 or more per day |
| <input type="checkbox"/> 1 per day            |  |

133. Over the past month, which of the following foods did you eat **AT LEAST THREE TIMES?**  
(**Mark all that apply.**)

- |   |   |
|---|---|
| <input type="checkbox"/> Avocado, guacamole                                   | <input type="checkbox"/> Olives                                 |
| <input type="checkbox"/> Cheesecake   | <input type="checkbox"/> Oysters                                |
| <input type="checkbox"/> Chocolate, fudge, or butterscotch toppings or syrups | <input type="checkbox"/> Pickles or pickled vegetables or fruit |
| <input type="checkbox"/> Chow mein noodles                                    | <input type="checkbox"/> Plantains                              |
| <input type="checkbox"/> Croissants   | <input type="checkbox"/> Pork neckbones, hock, head, feet       |
| <input type="checkbox"/> Dried apricots                                       | <input type="checkbox"/> Pudding or custard                     |
| <input type="checkbox"/> Egg rolls  | <input type="checkbox"/> Veal, venison, lamb                    |
| <input type="checkbox"/> Granola bars   | <input type="checkbox"/> Whipped cream, regular                 |
| <input type="checkbox"/> Hot peppers  | <input type="checkbox"/> Whipped cream, substitute              |
| <input type="checkbox"/> Jello, gelatin                                       |   |
| <input type="checkbox"/> Milkshakes or ice-cream sodas                        | <input type="checkbox"/> NONE                                   |

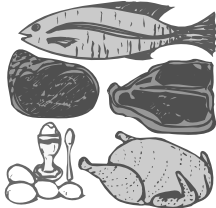
134. For **ALL** of the past 12 months, have you followed any type of **vegetarian diet**?

☐ NO (GO TO INTRODUCTION TO QUESTION 135)

☐ YES

134a. Which of the following foods did you **TOTALLY EXCLUDE** from your diet?  
(**Mark all that apply.**)

- ☐ Meat (beef, pork, lamb, etc.)  
☐ Poultry (chicken, turkey, duck)  
☐ Fish and seafood  
☐ Eggs  
☐ Dairy products (milk, cheese, etc.)



Introduction to Question 135 appears in the next column

**The next questions are about your use of fiber supplements or vitamin pills.**

135. Over the past 12 months, did you take any of the following types of **fiber or fiber supplements** on a regular basis (more than once per week for at least 6 of the last 12 months)?  
(**Mark all that apply.**)

- ☐ NO, didn't take any fiber supplements on a regular basis (GO TO QUESTION 136)  
☐ YES, psyllium products (such as Metamucil, Fiberall, Serutan, Perdiem, Correctol)  
☐ YES, methylcellulose/cellulose products (such as Citrucel, Unifiber)  
☐ YES, Fibercon  
☐ YES, Bran (such as wheat bran, oat bran, or bran wafers)

136. Over the past 12 months, did you take any **multivitamins**, such as One-a-Day-, Theragran-, or Centrum-type multivitamins (as pills, liquids, or packets)?

☐ NO (GO TO INTRODUCTION TO QUESTION 138)

☐ YES

137. How often did you take **One-a-day-, Theragran-, or Centrum-type** multivitamins?

- ☐ Less than 1 day per month  
☐ 1-3 days per month  
☐ 1-3 days per week  
☐ 4-6 days per week  
☐ Every day

137a. Does your **multivitamin** usually contain **minerals** (such as iron, zinc, etc.)?

- ☐ NO  
☐ YES  
☐ Don't know

137b. For how many years have you taken **multivitamins**?

- ☐ Less than 1 year  
☐ 1-4 years  
☐ 5-9 years  
☐ 10 or more years



Introduction to Question 138 appears on the next page

Over the past 12 months...

137c. Over the past 12 months, did you take any vitamins, minerals, or other herbal supplements other than your multivitamin?

☐ NO

Thank you very much for completing this questionnaire! Because we want to be able to use all the information you have provided, we would greatly appreciate it if you would please take a moment to review each page making sure that you:

- Did not skip any pages and
- Crossed out the incorrect answer and circled the correct answer if you made any changes.

☐ YES (GO TO INTRODUCTION TO QUESTION 138)

These last questions are about the vitamins, minerals, or herbal supplements you took that are NOT part of a One-a-day-, Theragran-, or Centrum-type of multivitamin.

Please include vitamins taken as part of an antioxidant supplement.

138. How often did you take **Beta-carotene** (NOT as part of a multivitamin in Question 137)?

☐ NEVER (GO TO QUESTION 139)

- ☐ Less than 1 day per month  
☐ 1–3 days per month  
☐ 1–3 days per week  
☐ 4–6 days per week  
☐ Every day

138a. When you took **Beta-carotene**, about how much did you take in one day?

- ☐ Less than 10,000 IU  
☐ 10,000–14,999 IU  
☐ 15,000–19,999 IU  
☐ 20,000–24,999 IU  
☐ 25,000 IU or more  
☐ Don't know

138b. For how many years have you taken **Beta-carotene**?

- ☐ Less than 1 year  
☐ 1–4 years  
☐ 5–9 years  
☐ 10 or more years

Question 139 appears in the next column

139. How often did you take **Vitamin A** (NOT as part of a multivitamin in Question 137)?

☐ NEVER (GO TO QUESTION 140)

- ☐ Less than 1 day per month  
☐ 1–3 days per month  
☐ 1–3 days per week  
☐ 4–6 days per week  
☐ Every day

139a. When you took **Vitamin A**, about how much did you take in one day?

- ☐ Less than 8,000 IU  
☐ 8,000–9,999 IU  
☐ 10,000–14,999 IU  
☐ 15,000–24,999 IU  
☐ 25,000 IU or more  
☐ Don't know

139b. For how many years have you taken **Vitamin A**?

- ☐ Less than 1 year  
☐ 1–4 years  
☐ 5–9 years  
☐ 10 or more years

140. How often did you take **Vitamin C** (NOT as part of a multivitamin in Question 137)?

☐ NEVER (GO TO QUESTION 141)

- ☐ Less than 1 day per month  
☐ 1–3 days per month  
☐ 1–3 days per week  
☐ 4–6 days per week  
☐ Every day

140a. When you took **Vitamin C**, about how much did you take in one day?

- ☐ Less than 500 mg  
☐ 500–999 mg  
☐ 1,000–1,499 mg  
☐ 1,500–1,999 mg  
☐ 2,000 mg or more  
☐ Don't know

140b. For how many years have you taken **Vitamin C**?

- ☐ Less than 1 year  
☐ 1–4 years  
☐ 5–9 years  
☐ 10 or more years

Question 141 appears on the next page

**Over the past 12 months...**

141. How often did you take **Vitamin E** (**NOT** as part of a multivitamin in Question 137)?

☐ NEVER (GO TO QUESTION 142)

- ☐ Less than 1 day per month
- ☐ 1–3 days per month
- ☐ 1–3 days per week
- ☐ 4–6 days per week
- ☐ Every day

141a. When you took **Vitamin E**, about how much did you take in one day?

- ☐ Less than 400 IU
- ☐ 400–799 IU
- ☐ 800–999 IU
- ☐ 1,000 IU or more
- ☐ Don't know

141b. For how many years have you taken **Vitamin E**?

- ☐ Less than 1 year
- ☐ 1–4 years
- ☐ 5–9 years
- ☐ 10 or more years

142. How often did you take **Calcium** or **Calcium-containing antacids** (**NOT** as part of a multivitamin in Question 137)?

☐ NEVER (GO TO QUESTION 143)

- ☐ Less than 1 day per month
- ☐ 1–3 days per month
- ☐ 1–3 days per week
- ☐ 4–6 days per week
- ☐ Every day

142a. When you took **Calcium** or **Calcium-containing antacids**, about how much elemental calcium did you take in one day?  
(If possible, please check the label for elemental calcium.)

- ☐ Less than 500 mg
- ☐ 500–599 mg
- ☐ 600–999 mg
- ☐ 1,000 mg or more
- ☐ Don't know

142b. For how many years have you taken **Calcium** or **Calcium-containing antacids**?

- ☐ Less than 1 year
- ☐ 1–4 years
- ☐ 5–9 years
- ☐ 10 or more years

**The last two questions ask you about other supplements you took more than once per week.**

143. Please mark any of the following **single supplements** you took more than once per week (**NOT** as part of a multivitamin in Question 137):

- |  |  |
|--|--|
| <input type="checkbox"/> B-6                   | <input type="checkbox"/> Folic acid/folate       |
| <input type="checkbox"/> B-complex             | <input type="checkbox"/> Glucosamine             |
| <input type="checkbox"/> Brewer's yeast        | <input type="checkbox"/> Hydroxytryptophan (HTP) |
| <input type="checkbox"/> Cod liver oil         | <input type="checkbox"/> Iron                    |
| <input type="checkbox"/> Coenzyme Q            | <input type="checkbox"/> Niacin                  |
| <input type="checkbox"/> Fish oil              | <input type="checkbox"/> Selenium                |
| <input type="checkbox"/> (Omega-3 fatty acids) | <input type="checkbox"/> Zinc                    |

144. Please mark any of the following **herbal** or **botanical supplements** you took more than once per week.

- |   |  |
|---|--|
| <input type="checkbox"/> Aloe Vera            | <input type="checkbox"/> Ginger                      |
| <input type="checkbox"/> Astragalus           | <input type="checkbox"/> Ginkgo biloba               |
| <input type="checkbox"/> Bilberry             | <input type="checkbox"/> Ginseng (American or Asian) |
| <input type="checkbox"/> Cascara sagrada      | <input type="checkbox"/> Goldenseal                  |
| <input type="checkbox"/> Cat's claw           | <input type="checkbox"/> Grapeseed extract           |
| <input type="checkbox"/> Cayenne              | <input type="checkbox"/> Kava, kava                  |
| <input type="checkbox"/> Cranberry            | <input type="checkbox"/> Milk thistle                |
| <input type="checkbox"/> Dong Kuai (Tangkwei) | <input type="checkbox"/> Saw palmetto                |
| <input type="checkbox"/> Echinacea            | <input type="checkbox"/> Siberian ginseng            |
| <input type="checkbox"/> Evening primrose oil | <input type="checkbox"/> St. John's wort             |
| <input type="checkbox"/> Feverfew             | <input type="checkbox"/> Valerian                    |
| <input type="checkbox"/> Garlic               | <input type="checkbox"/> Other                       |

**Thank you very much for completing this questionnaire! Because we want to be able to use all the information you have provided, we would greatly appreciate it if you would please take a moment to review each page making sure that you:**

- Did not skip any pages and
- Crossed out the incorrect answer and circled the correct answer if you made any changes.

Question 143 appears in the next column